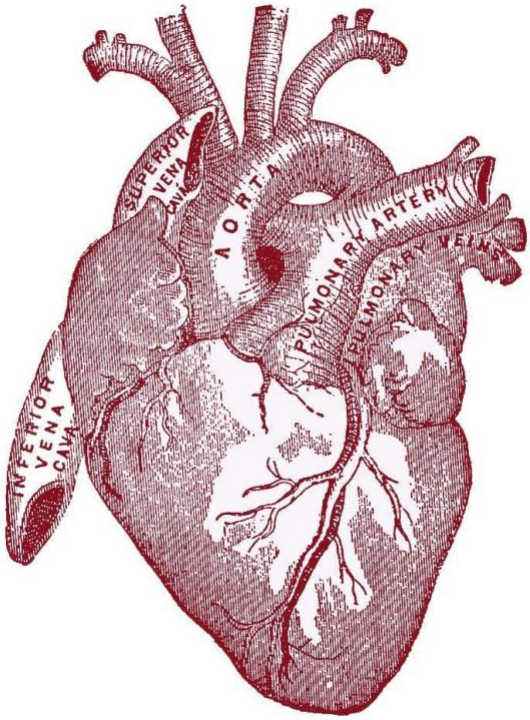
The Red Book

Housestaff Manual for Cardiology



Department of Medicine
Massachusetts General Hospital
Harvard Medical School
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Editors
Krishan Sharma, MD
Christopher Marnell, MD

LETTER FROM THE EDITORS

It is our honor to present the 2022-2023 edition of the Housestaff Manual for Cardiology. Former MGH house officer, Andrew Sauer, spearheaded the first edition in 2010, with the intention of offering residents a practical introduction to the major concepts essential to everyday patient care in the Coronary Care Unit (CICU) and the cardiac Step Down Unit (SDU).

Continuing the efforts of last year's edition, we hope to present a Red Book that provides an up-to-date, comprehensive review of core Cardiology topics, yet in a format accessible enough for the busy resident to pick up and extract critical teaching points to inform their patient care – the core mission the Red Book has always sought to fulfill.

In 1994, based on the understanding that exceptional patient care is grounded in a rich foundation of evidence, Albert Shaw and Ravi Thadhani set out to create a reference guide for residents that compiled up-to-date guidelines for clinical management. This resource, entitled "The MGH Department of Medicine Housestaff Manual," has since been updated annually and represents the rigor, autonomy, and pride with which our residents approach their work. We intend for "The Red Book" to encapsulate these same principles within the field of cardiology and to pay tribute to the original DOM housestaff manual, now in its 26th year, and known more affectionately as "The White Book."

This commitment to well-informed practice is grounded in a genuine desire to understand, connect with, and improve the lives of our patients, but a more difficult reality emerges when we feel that our efforts have fallen short. As agents of medical practice, we continuously engage with elusive concepts—illness, intimacy, loss, grief—and wrestle to ascribe meaning to the intangible. In the year 1980, Dr. Ted Stern, an MGH psychiatrist and the psychiatric consultant to the medical intensive care unit (MICU), attempted to confront and respond to these challenges when he purchased a journal, the cover of which was red, and placed it in the MICU. From then, until 2003, the red book served as a collective forum for resident self-reflection. It supplemented his weekly "autognosis" (self-knowledge) rounds. After it was filled, seven more volumes followed. Excerpts from the journals were subsequently complied and incorporated into a book, "On the Edge of Life: Diary of a Medical Intensive Care Unit" edited by Drs. Mikkael Sekeres (a former MGH house officer) and Ted Stern. While Dr. Stern's "Red Book" is no longer in existence, its spirit is still very much alive at MGH, particularly on our cardiology rotations and exemplified by Dr. Hasan Bazari's CICU reflection rounds. We hope that this guide will serve as another reminder to carve out space for introspection and to allow for the projection of kindness and empathy both inward and outward.

In addition to the individuals mentioned above, we would like to thank the many current and former MGH housestaff and faculty who have updated and provided original contributions to this guide. We are deeply appreciative of their dedication, leadership, and commitment, without which "The Red Book" would not be possible.

The following attending reviewers have provided expert opinion and consultation for past and present editions of the Red Book:

Kevin Heist
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We would also like to acknowledge the outstanding leadership of our section editors (bold) and content writers:

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Krishan Sharma	Vascular Medicine
Chris Marnell, Max Quinn	Adult Congenital Heart Disease
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Finally, we would like to provide a special thank-you to Dr. Dave Dudzinski, Dr. Jay Vyas, the DOM Chief Residents, and the DOM Staff for supporting our endeavor.

We hope that this guide will continue to assist with the care of cardiac patients at MGH. As such, it is meant to serve as a reference to be used in conjunction with other resources and never in place of sound clinical judgment. Thank you for continuing to provide the highest level of care and compassion to our patients.

Krishan Sharma, MD
Christopher Marnell, MD
The Red Book Editors
2021-2022

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INTRODUCTION TO INPATIENT CARDIOLOGY

CCU & SDU Rotation Overview

Heart Center Overview: The MGH Corrigan Minehan Heart Center comprises 5 inpatient units. Residents rotate in two (see below)

- Blake 8 Cardiac surgical ICU
- Ellison 8 Cardiac surgical Step-Down Unit
- Ellison 9 CCU (residents)
- Ellison 10 Cardiac Step-Down (residents)
- Ellison 11 Cardiac "Access" Unit

Introduction to the Ellison 9 CCU:

- 16 bed ICU staffed by distinct **Red** and **Blue** teams
- Triage decision re: Red v Blue made by HCICU intensivist (some fluidity based on overall team census and attending preferences)

	Staffing	Team Cap	Case Mix
CCU Red	● HCICU intensivist ● APP ● Heart Failure consult team ● IM resident(s) on elective	-	● Post-op cardiac surgery ● Advanced HF pts pre/post VAD ● Advanced HF pts pre/post-transplant ● Cardiogenic shock requiring temporary MCS
CCU Blue	● CCU Attending* +/- MICU attending ● MGH/Brigham cardiology fellow ● SAR ● 4 JARs	12 (hard cap)	● ACS (no MCS) ● Unstable arrhythmia ● Severe valvulopathy ● Pericardial disease ● Post-cardiac arrest ● Cardiogenic shock (no MCS) ● MICU 'boarders'

*****Blue attending is often a cardiologist without specific critical care training, may consult the HCICU intensivist for input re: ventilation, sedation etc.

CCU Blue Team Roles:

- **SAR**: Primarily responsible for leading rounds, maintaining the handoff, supervising procedures, interfacing with families, and running codes
- **JARs**: Rotate through a q4 call schedule as detailed below (Call->Post->Swing->Pre/Plan). Responsibilities include admitting patients, performing procedures, running plan on rounds, and doing swing.
- **Call JAR**: Arrives at ~7am and admits until team arrives at 7a the next day, except for new patients that arrive during rounds if there is a swing JAR present (goal is to keep call JAR on rounds to understand plans and contingencies going into the night). Depending on attending preference, will usually check in with CCU attending by phone around ~10pm. Sends 5am email and leaves after presenting new admissions on team rounds at 8a.
- **Swing JAR:** Arrives at ~7am, protects rounds by admitting new patients that arrive during rounds and performing swing tasks including procedures (depending on experience/comfort). Usually stays through PM rounds
- **Pre/Plan JAR:** Presents established patients on rounds and signs progress notes. Leaves first, often before PM rounds. Usually has one afternoon of clinic during the block. Performs afternoon swing tasks if Swing resident is off

Codes in the CCU:

- **Day:** Run by the native CCU Blue SAR (with support from the CCU fellow, Senior On, and JARs)
- **Night:** Run by the cardiology night teach/Senior On or overnight fellow (OA will page Senior On/Cardiology Night Team, fellow/call JAR runs the code until NT arrives)

Codes outside the CCU:

- **Day:** Call JAR goes to codes on the floors--primary responsibilities are to monitor pulse, place I/O (will be brought by the MICU intern) and assist as otherwise directed by the senior on/code whisperer.
- **Night:** Call JAR does not go to codes since they are the only resident on the floor

Overnight Support: There are many layers of overnight support in the CCU, each useful in different circumstances

- **Cardiology Night Teach:** Beginning in AY 2021-2022 there will be a dedicated NT for the CCU and SDU. Can be contacted for procedural supervision, general cardiology, or critical care questions, or if needing support for admissions (NT can either help stabilize patients or coordinate with chiefs to hit in an additional admitting resident). **The Cards NT is also responsible for running codes in the CCU overnight and will be paged by the OA**
- **Overnight Cardiology Fellow:** There is now an **in-house** 1st or 2nd year cardiology fellow who covers the CCU and SDU in addition to seeing consults on the floors/ED and performing STAT TTEs. The fellow should be first call for issues with Blue team patients and can help mobilize other cardiology resources as needed (i.e., cath lab, temp wires, etc.) and guide outreach to other subspecialists overnight.
- **Access Fellow:** Dedicated **in-house** fellow who covers the Ellison 11 Access Unit and is first-call for access site complications on cardiac patients across the hospital (bleeding, suspected ischemia distal to access site, any questions about TR bands, etc.). They will come hold pressure for access site bleeds (resident not expected to hold pressure for prolonged periods) and will help direct further management.
- **CCU Attending:** The native CCU Blue attending can and should be contacted for high-level management questions on established Blue patients, particularly if there is disagreement with the overnight fellow or if a patient is complex (the overnight fellow most often will not know the patients). Most attendings will plan a scheduled phone check-in at ~10pm but will remain available thereafter. The Blue attending should also be contacted if needing to involve the HCICU intensivist or Shock team overnight.
- **HCICU intensivist:** Available **in-house** overnight and can be consulted for critical care issues on Blue team patients (need for intubation, vent/sedation issues, difficult procedures, troubleshooting mechanical support devices). Also holds the Shock/ECMO consult pager and is responsible for Blue/Red triage decisions.
- **Overnight Intensivist: In-house** intensivist covering **MICU boarders** in the CCU (for critical care questions on CCU Blue team cardiology patients, contact the HCICU intensivist). Available for general management questions, to supervise procedures, to staff new MICU admissions.
- **CCU Red APP:** Cardiac surgery PA/NP who sits in the Red Team office near the double doors at the CCU entrance. Can be a useful resource for questions regarding post-op patients and for help troubleshooting MCS devices.

Tips for CCU Admission/ Presentation:

- Provide the cardiac history in chronological order
- Have details on prior cardiac studies available
- **Treadmill stress test:** remember to include duration of exercise, METS achieved, HR (and % maximum), BP, peak double product (“good test” > 20k), EKG/imaging
- **Echo:** TTE or TEE, EF, valves, wall motion abnormalities, wall, and cavity dimensions (IVS, LVID) and atrial dimensions
- **Catheterizations:** Go anatomically! Right heart cath values first in the order obtained (RA, RV, PA, PAOP), then LV gram results, then coronary angiography (Left main, LAD, LCx, RCA) finally, interventions and complications
- **CABG:** anatomy is critical; if OSH surgery, you must obtain a copy of the operative report or post-CABG angiogram
- Print relevant EKGs (including a baseline) for review on rounds

Tips for daily CCU rounds:

- Ensure each patient has daily EKG, and ideally print them (SAR can choose whether plan/call/swing JAR does this)
- Find patient’s RN prior to rounding on each patient (often Swing JAR task)
- Engage nursing at bedside, similar to MICU rounds
- Offer a suggested plan but recognize these patients are complicated, and often there are many possible approaches

Introduction to the Ellison 10 SDU: Ellison 10 is a 36-bed cardiology unit which admits patients with primary cardiac disorders and serves as a step-down unit for the Ellison 9 CCU. Patients in the SDU are cared for by two equivalent housestaff teams (Red and Blue) and an EP team.

SDU Team Structures: Each team is composed of 1-2 day interns, 2 JARs, 1 SAR, and 1 attending. There is also an embedded cardiology fellow dedicated to teaching both teams. The Blue and Red teams alternate admitting days. The JAR admitting cycle is: long rounding – long admit – short rounding – short admit.

Admitting Team roles:

- **Day intern**: pre-rounds on 2-4 patients with SAR supervision and presents at 8 am rounds. Assigned 1-2 admissions during the day that are supervised by the SAR and formally staffed in the afternoon.
- **Short admit JAR:** Arrives at 7 am signs into admitting pager (31010), pre-rounds on list, and card-flips patients following presentation of overnight admissions. Admits 3 patients until 3:00 pm. The first admission of the day will typically go to the day intern. Short Call admissions should be staffed with the attending on the day the patients are admitted, if possible. They sign out to the SAR (if finished before 7:00 pm) or the NF JAR (if finished at 7:00pm).
- **Long admit JAR**: Arrives at 7 am and card-flips patients after short admit JAR. Begins admitting at 3 pm (or earlier of short admit is capped) and can admit up to 4 patients before 7 pm. Admissions not staffed the same day will be passed off to the NF team and formally presented the following morning. Any admissions over-cap will be passed off and stabilized by the Long SAR and passed off to the NF team.
- **Long SAR**: supervises admissions, oversees discharges,

Rounding Team roles:

- **Day intern**: rounds on their list of 2-4 patients and may sign out to Long rounding JAR when swing is complete
- **Short rounding JAR**: Arrives at 7 am, pre-rounds, and presents any new patients from prior day (when they were Long admit JAR) at morning rounds, may pass off their list to Long rounding JAR when swing is complete
- **Long rounding JAR**: Arrives at 7 am, pre-rounds on patients and card-flips after new patient presentations. Takes pass off from the Day Intern and Short Rounding JAR once they are done with swing and ready to pass off. If the EP team is available to pass off prior to 7 pm, they will pass off to the Long Rounding JAR to pass off to the NF JAR. The Long Rounding JAR passes off to the NF team
- **Short SAR**: supervises day intern rounds, attends case management rounds at 10:30 am oversees discharges

Overnight Support: please refer to the SDU Night Float guide for full details

- Cardiology Night Teach will see and staff all admissions performed by SDU NF interns (JAR does not have to formally staff)
- For access site issues Access fellow
- For acute clinical change requiring a cardiologist within 30 minutes in-house cardiology fellows
- For EP patients EP Fellow, they may independently request assessment by other in-house cardiology staff

Overview of Cardiac Procedures Relevant to CCU/SDU Patients:

Coronary angiography +/- PCI:

- Indications: Acute coronary syndromes, chronic coronary syndromes refractory to medical therapy or with high-risk features, workup of heart failure or unexplained ventricular tachycardia, others
- Procedure overview: Arterial access established via radial or femoral arteries, coronary ostia engaged with catheters and angiogram performed with injection of iodinated contrast under fluoroscopy. Functional assessment of stenotic lesions sometimes performed with fractional flow reserve (FFR) or instant wave free ratio (iFR) techniques. If indicated, stents will then be deployed, and the patient loaded with a P2Y12 inhibitor.
- Pre-procedure planning:
- NPO @ MN
- Anti-coagulation management (source: MGH Cardiac Cath Lab Anticoagulation Guidelines, available on Ellucid)

- Questions for pass-off: **Procedure** (diagnostic findings and interventions), **Access** (Where and what size access was used? High stick? Do you want the sheaths pulled? When? By whom? At what PTT? Duration of bedrest? Closure devices used? TR band in place?), **Anticoagulation** (What was used in the case? Do you want heparin or bivalirudin restarted?), **Antiplatelets** (Was the patient loaded with a P2Y12? What should be ordered going forward?) **Complications**?
- Post-procedure evaluation: Check groin yourself for expansile mass, tenderness, bruit (suggestive of pseudoaneurysm). Document full bilateral neurovascular exam
- Key complications to watch out for: Access site bleeding, retroperitoneal hematoma, arterial pseudoaneurysm, limb ischemia, coronary perforation resulting in tamponade
- Contingencies: For an acute access site bleed, **hold pressure** proximal to arteriotomy (several cm proximal to skin puncture), page fellow who performed procedure (day) or cardiac access fellow (night)

For any procedural/access questions, first port-of-call for help should be cardiology or interventional cardiology fellow.

Right Heart/Pulmonary Artery Catheterization

- Indications: Suspected cardiogenic shock, pulmonary hypertension, pericardial disease, worsening renal function in decompensated HF, others
    - Must be inserted in cath lab (rather than bedside) if: LBBB, severe PH (PAP>70mmHg), large RV, PPM/ICD, temp wire, severe TR, prosthetic TV/PV
    - Contraindications: RA/RV mass/thrombosis, mechanical TV/PV, endocarditis (TV/PV)
- Procedure Overview: ~8Fr venous sheath ("Cordis") inserted under ultrasound guidance in central vein (RIJ>LIJ>L subclav>femoral), pulmonary artery catheter inserted into SVC, balloon tip inflated, catheter advanced under fluoroscopy or while monitoring hemodynamic waveforms until wedge tracing obtained, balloon deflated, line then removed or secured in place
- Pre-procedure Planning:
    - NPO @ MN
    - Considered a "low bleeding risk" procedure (relative to procedures requiring arterial access), though anticoagulants should still be held per the MGH cath lab anticoagulation guidelines listed above
    - Need to decide and communicate to cath lab whether you want a one-time diagnostic RHC or "PA line to stay"--note that PA catheters only allowed in the CCU and Ellison 11.
- Questions for pass-off: **Results** (i.e. hemodynamics measurements--be sure to note whether reported values were taken at end-expiration or as the mean value across the respiratory cycle), **Access** (Where and what size? Sheath still in place? Should they be pulled? By whom? At what PTT? Activity restrictions?), **Anticoagulation** (when to restart), **Complications**
- Post-procedure evaluation: Examine access site, if line left in place ensure balloon deflated and obtain CXR (waveform more useful than CXR to assess initial position but helpful to have a baseline in case of issues later)
- Key complications to watch out for: infection, bleeding, PTX, VT, RBBB, CHB, PA rupture (place patient on side with the catheter “bleeding side down”, order STAT CXR, CBC, coags, CT surgery consult), pulmonary infarct, PE

TAVR (Transcatheter aortic valve replacement):

- Indications: Severe aortic stenosis with symptoms or other high-risk features (see Aortic Stenosis section for full list of indications)
- Procedure Overview: Femoral artery access obtained using a 14F sheath or greater, transvenous access obtained and RV pacing wire placed, guide wire placed across aortic valve and dilation performed, prosthesis moved into position under fluoro + TEE or TTE guidance, rapid ventricular pacing (>180bpm) initiated to decrease stroke volume, allowing valve to be deployed. Valve either self-expands (Medtronic CoreValve) or is expanded with a balloon (Edwards Sapien).
- Pre-procedure Planning:
    - Standard pre-TAVR workup: TTE, coronary angiography +/- RHC, carotid duplex, CT surg consult, Panorex + dental evaluation
    - Note presence of pre-existing conduction disease, increasing the likelihood of pt requiring PPM post-TAVR
    - NPO @ MN for procedure
    - Anesthesia plan (MAC vs general)
- Questions for pass-off: **Results** (successful? Type and size of valve? Presence of paravalvular leak?), **Access** (Where and what size? Sheath still in place? Should they be pulled? By whom? At what PTT? Activity restrictions?), **Anticoagulation** (when to restart), **Antiplatelets** (what is antiplatelet plan? typically DAPT) **Complications** (Access site bleeding, paravalvular leak, new/worsening heart block)
- Post-procedure evaluation: Examine access sites, document peripheral pulses, EKG to assess for new/worsening heart block, screening neuro exam
- Key complications:
    - "Big 5" TAVR Complications: Bleeding, stroke, paravalvular leak (PVL), AKI, Complete Heart Block
    - "Suicide LV": Acute LVOT obstruction resulting from relief of fixed afterload which unmasks increased contractility from chronically hypertrophied ventricle, resulting in reduced CO and shock (treat similar to hypertrophic cardiomyopathy with LVOT obstruction, i.e. fluids, beta blockers, phenylephrine)
    - Differential for shock after TAVR: Bleeding, aortic annular rupture, severe PVL, acute MI from inadvertent occlusion of coronary ostia, suicide LV (examine access sites, EKG, stat TTE)

Pulmonary vein isolation:

- Indications: Symptomatic atrial fibrillation with failure or intolerance of anti-arrhythmic drugs
- Procedure Overview: Bilateral femoral venous access obtained, ablation catheters inserted from the RA->LA via atrial septal puncture, pulmonary veins isolated via radiofrequency or cryoablation. Additional lesions sometimes created such as with a posterior wall isolation. Venous access sites often occluded with sutures locked in place via stopcocks.
- Pre-procedure Planning: Patients typically brought in by EP as outpatients then admitted to the SDU for one night post-procedurally
- Questions for pass-off: **Results** (PVI alone or additional lesions?) **Access and closure technique** (typically b/l femoral veins occluded with stopcocks), **Anticoagulation** (when to restart patient's DOAC or warfarin), **Complications** (any concern for perforation or effusion? TTE performed during procedure?) **Meds:** (Pred taper? Sucralfate?)
- Post-procedure evaluation: Examine groin sites, ensure stable blood pressure (high index of suspicion for perf+tamponade)
- Key complications to watch out for:
    - Acute: Access site bleeding, stroke, perforation + tamponade (resulting from excessive overheating of atrial tissue or catheter puncture)
    - Subacute: atrio-esophageal fistula (presents with sepsis, endocarditis, air emboli, or GI bleeding 1-6 weeks after PVI), pulmonary vein stenosis (dyspnea, cough, hemoptysis 2-5 mo after PVI)
    - For any significant or sustained hypotension following PVI, page EP for consideration of formal TTE to r/o tamponade (EP will either do it themselves or ask gen cards fellow to do so)

ACUTE CORONARY SYNDROMES AND ISCHEMIC HEART DISEASE

If you suspect ST-elevated myocardial infarction (STEMI) in an admitted patient:

- Call a **Rapid Response**
- If true STEMI, call **6-8282**. This puts you in touch with the interventional attending (if after hours) or the cath lab charge RN (if during business hours), who can help guide the next steps (i.e. cath lab activation)
- If there is uncertainty about the ECG meeting STEMI criteria, STAT page the general cardiology fellow on call.

On-call cardiology assignments can also be viewed through amion.com, password mghcard

Classification

Angina pectoris: Chest pain caused by myocardial oxygen demand outstripping myocardial oxygen supply.

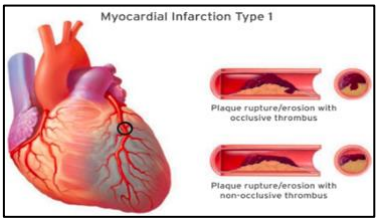
- Classically: 1) Substernal, 2) Worsened with exertion, 3) Relieved by rest or nitroglycerin
- Stable angina: Occurs predictably at a certain level of exertion and is relieved with rest or nitroglycerin

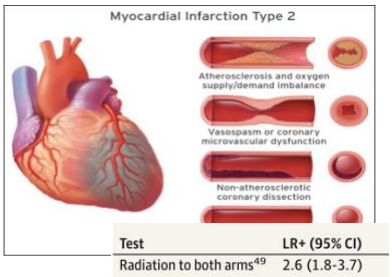
Acute coronary syndrome (ACS) This is commonly subdivided into non-ST-elevation ACS (NSTE-ACS) – including unstable angina or NSTEMI – or STEMI. Important features that can distinguish NSTE-ACS from stable CAD.

  - Rest angina, which is usually more than 20 minutes in duration
  - New onset angina that markedly limits physical activity
  - Angina that is more frequent, longer in duration, or occurs with less exertion than previous angina
- STEMI: Designates an MI in patients with chest discomfort or other ischemic symptoms, who develop EKG changes denoted in "Diagnosis" Section. Often denotes acutely occluded coronary artery from thrombus arising from plaque disruption or erosion or rarely thromboembolism
- NSTEMI: MI without ST-segment elevation
- Unstable angina: ACS without biomarker elevation

Joint Task Force Classification of Myocardial Infarction JACC 2018;72(18):2231-2264:

- **Type 1:** Spontaneous MI**.** Atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection causing intraluminal thrombus in 1+ coronary arteries.
- **Type 2:** Demand MI. Myocardial injury *with* necrosis in which a condition *other than CAD* contributes to an imbalance between myocardial O_2- supply and demand
- **Type 3:** MI resulting in death but biomarkers unavailable with symptoms suggestive of MI including new ischemic ECG changes or new LBBB
- **Type 4a:** MI related to PCI **(**with cTn > 5x 99th-percentile URL)
- **Type 4b:** MI related to stent thrombosis.
- **Type 4c:** MI related to PCI after initial successful PCI due to restenosis or complex PCI
- **Type 5:** MI related to CABG (with cTn > 10x 99th-percentile URL)





History

When evaluating patients with chest pain for ACS:

- **Typical ischemic chest pain:** Commonly meets angina characteristics. OPQRST mnemonic:
  - Onset: Gradual
  - Provocation/palliation: Provoked by an activity; not changed with respiration or position
  - Quality: Substernal pressure (squeezing, burning or tightness)
  - Radiation: Radiates to the shoulder, neck, jaw, or either arm (may also be inter-scapular or epigastric)
  - Site: Not felt in one specific spot, but diffuse discomfort
  - Time course: Angina (2-5 min),
- **Atypical chest pain:** Falls short of meeting all three criteria
  - Common presentation of ACS, with 10% of individuals reporting dyspnea alone.
  - More common in women, elderly, inferior MI, and patients with diabetes
  - May rarely present with fatigue, lethargy, syncope, AMS, CVA/TIA, or GI distress
- **Non-ischemic chest pain:**
  - Quality: Pleuritic, sharp, or reproducible with palpation
  - Timing: Occurring with cessation of exercise or lasting only seconds or >6 hrs.
  - Context: Without evidence of myocardial damage by biomarkers. Chest pain that is not ischemic may represent other life-threatening etiologies of chest pain, such as aortic dissection, PE, or pneumothorax. Alternative diagnoses should be ruled out before disregarding chest pain.

Test	LR+ (95% CI)
Radiation to both arms[49]	2.6 (1.8-3.7)
Pain similar to prior ischemia[49]	2.2 (2.0-2.6)
Change in pattern over prior 24 h[49]	2.0 (1.6-2.5)
"Typical" chest pain[d,47,49,54,60,62,71]	1.9 (0.94-2.9)
Worse with exertion[e,49,73]	1.5-1.8
Radiation to neck or jaw[37,49,60]	1.5 (1.3-1.8)
Recent episode of similar pain[73]	1.3 (1.1-1.4)
Radiation to left arm[37,47,49]	1.3 (1.2-1.4)
Radiation to right arm[49]	1.3 (0.78-2.1)
Associated diaphoresis[e,49,60]	1.3-1.4
Associated dyspnea[49,60,62]	1.2 (1.1-1.3)
Abrupt onset[49]	1.1 (1.0-1.2)
Any improvement with nitroglycerin[40,66,73]	1.1 (0.93-1.3)
"Typical" radiation[e,f,54,62]	1.0-5.7
Burning pain[e,49,60]	1.0-1.4
Associated nausea/vomiting[e,49,60]	0.92-1.1
Associated palpitations[60]	0.71 (0.37-1.3)
Associated syncope[73]	0.55 (0.39-0.76)
Pleuritic pain[e,37,49]	0.35-0.61

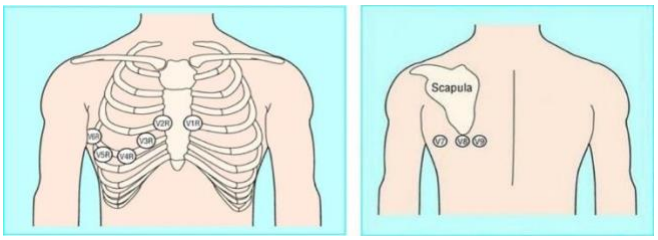
Diagnosis

A. Physical Exam: Exam findings do not predict ACS reliably

- Signs w/ high pre-test probability for CAD: S4, Levine's sign, signs for disease in other vascular beds
- High-risk features in ACS: syncope, new HF (S3 gallop, rales, or elevated JVP), possible mechanical complication such as papillary muscle or ventricular septal rupture (sinus tachycardia, hypotension, elevated JVP, or new systolic murmur)

B. 12-lead ECG: 50% of patients with MI have a normal or non-diagnostic ECG on presentation, repeat q10-15m if ongoing sx

a. Right sided leads: For RV infarction. Inferior STEMI + V1 STE +/- V2 STD
b. Posterior leads: For posterior MI. STDs in V1-V3, R/S ratio >1 in V1-V2



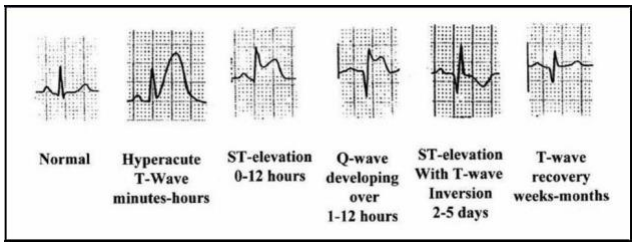
(*Left*) Right-sided leads, (*Right*) Posterior leads

NSTEMI ECG Criteria:

- New horizontal or down-sloping **STD of ≥ 0.5mm**
- **TWI ≥ 0.1mm** with a **prominent R-wave or R/S ratio > 1** in ≥ 2 contiguous leads

STEMI ECG Criteria: (≥1 of the following)

- **New STE:** measure ST segment 80ms (2 small boxes) from the J-point (inflection point between S-wave and ST segment) in 2 contiguous leads
  - Pathologic elevations ≥ 1 mm except V2, V3 (M: ≥ 2 mm, F ≥ 1.5)
  - **Patients may demonstrate elevations in the anterior precordial leads (V1–V3) which is NOT pathologic*[2]
- **New LBBB**
- **Posterior MI** defined by STD in ≥2 V1–V4. Check posterior leads

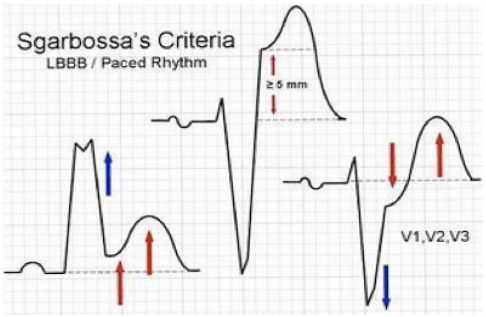


ECG evolution in STEMI

Sgarbossa Criteria: Used to diagnose AMI in LBBB/Paced Rhythm

- Normal: ST segment should be discordant with the QRS complex.
- Sgarbossa criteria:
  - STE > 1mm concordant with QRS in any lead = 5 points
  - STD > 1mm concordant with QRS in V1, V2 or V3 = 3 points
  - STE > 5mm *discordant* with QRS in any lead = 2 points

Total Sgarbossa criteria point score ≥ 3 yields 90% specificity and 88% PPV for MI, but notably only a sensitivity of 20%.[3]



Localization of Injury (Zimetbaum et al. NEJM 2003;348)

- Contiguous STE may indicate which vessel is involved.
- STE correlate better with a vascular territory than STD or TWIs.

Category	Anatomy of Occlusion	ECG Findings
Proximal LAD (antero-lateral MI)	Prox to 1st septal perforator	STE V1–6, I, aVL +/– BBB
Mid-LAD (antero-lateral MI)	Distal to 1st septal perforator, prox to 1st diag	STE V1–6, I, aVL
Distal LAD/Diag (apical MI)	Distal to diagonal or diagonal itself	STE V1–6 or I, aVL, V5–6
High Lateral MI	Proximal LCx	STE I, aVL +/– V5, V6
"Apical" MI (Low lateral MI)	Distal LCx	STE V5, V6
Large Inferior MI	Proximal RCA (90%) or LCx (10%)	STE II, III, AVF *and:* 1. V1, V3R, V4R *(RV)* 2. V5-V6 *(inferoapical)* 3. R>S V1-2, STD V1-V3, STE V8 *(inferoposterior)*
Small Inferior MI	Distal RCA, LCx branch	STE II, III, aVF

Critical Left Main Dz	Left main	STE >1 mm in aVR AND STE in aVR > V1 OR widespread STD

Other Notable ECG patterns:
Pre-existing RBBB: Terminal ST-segments should not be affected by RBBB. Interpret ischemia on ECG as if no BBB. If deep discordant STD in V1-V3, check posterior leads.
deWinter's T-waves (2% of STEMIs): Tall symmetric T-waves + >1mm STD at J-point in precordial leads + 0.5-1mm STE in aVR, may evolve to STEs, consistent w/ acute LAD occlusion.
Wellen's Pattern: Biphasic T waves (25%; Type A) or symmetric, deeply inverted T waves (75%; Type B) in V2, V3
Wellen's Syndrome: Wellen's pattern in patients with resolved CP indicates reperfusion of myocardium consistent with acute LAD occlusion. 75% of pts will have anterior MI in days to weeks if not treated. *Do not stress these patients.*

- *DDx Wellen's*: apical HCM, coronary vasospasm, elevated ICP (long QTc), MI, PE, post-tachycardia/pacing, BBB, WPW, idiopathic.

DDx ST Elevations		DDx ST Depressions
Acute MI	Takotsubo/stress cardiomyopathy	Ischemia, NSTEMI
Vasospastic Angina	Massive PE (V1, V2 occasionally)	Posterior wall MI
Benign Early Repolarization	Brugada pattern (V1–V3 with RBBB)	Digoxin effect
Acute Pericarditis	Tumor or Trauma	Pericarditis
LVH or LBBB	V-paced rhythms	LVH or LBBB
LV Aneurysm	Hypothermia (Osborn/J wave)	LV Aneurysm
Myocarditis	Post-DC cardioversion (rarely)	Myocarditis
Hyperkalemia (V1, V2)	Hypercalcemia (rarely)	Hypokalemia

C. Cardiac Biomarkers

Troponin: At MGH, use a high-sensitivity troponin T (hsTnT) assay. An elevated troponin is defined as: hsTnT ≥10 ng/L (in F) and ≥12 ng/L (in M).

- Peaks within 12-48 hours and returns to normal within 5-14 days. Reaches peak more quickly when revascularized, more slowly when not.
- Converting numbers between assays (4^{th} generation to hsTnT assay): for > 0.01 multiply by 1000 to get hsTNT
  - For values < 0.1, remember: cTnT value of 0.01 ng/ml hsTnT of 30 ng/L, 0.03 ng/ml hsTnT of 53 ng/L

How to Use hsTnT:

- DO NOT wait for troponin if high suspicion for ACS (classic pain, ECG changes) immediately start treatment
- Order troponin at presentation + 3hr repeat. Check after 1hr if worried
- A rising *OR* falling value (delta) ≥ 5 w/ symptoms or ECG changes consider ACS.
- If baseline troponin >99^{th} percentile (more common in CKD or left ventricular hypertrophy patients; mechanism of action (MOA) not completely understood), a rise and fall of 20% is suggestive of MI. As with the general population and hsTnT, the "delta" in troponin values is critical to determine the likelihood of an acute coronary syndrome

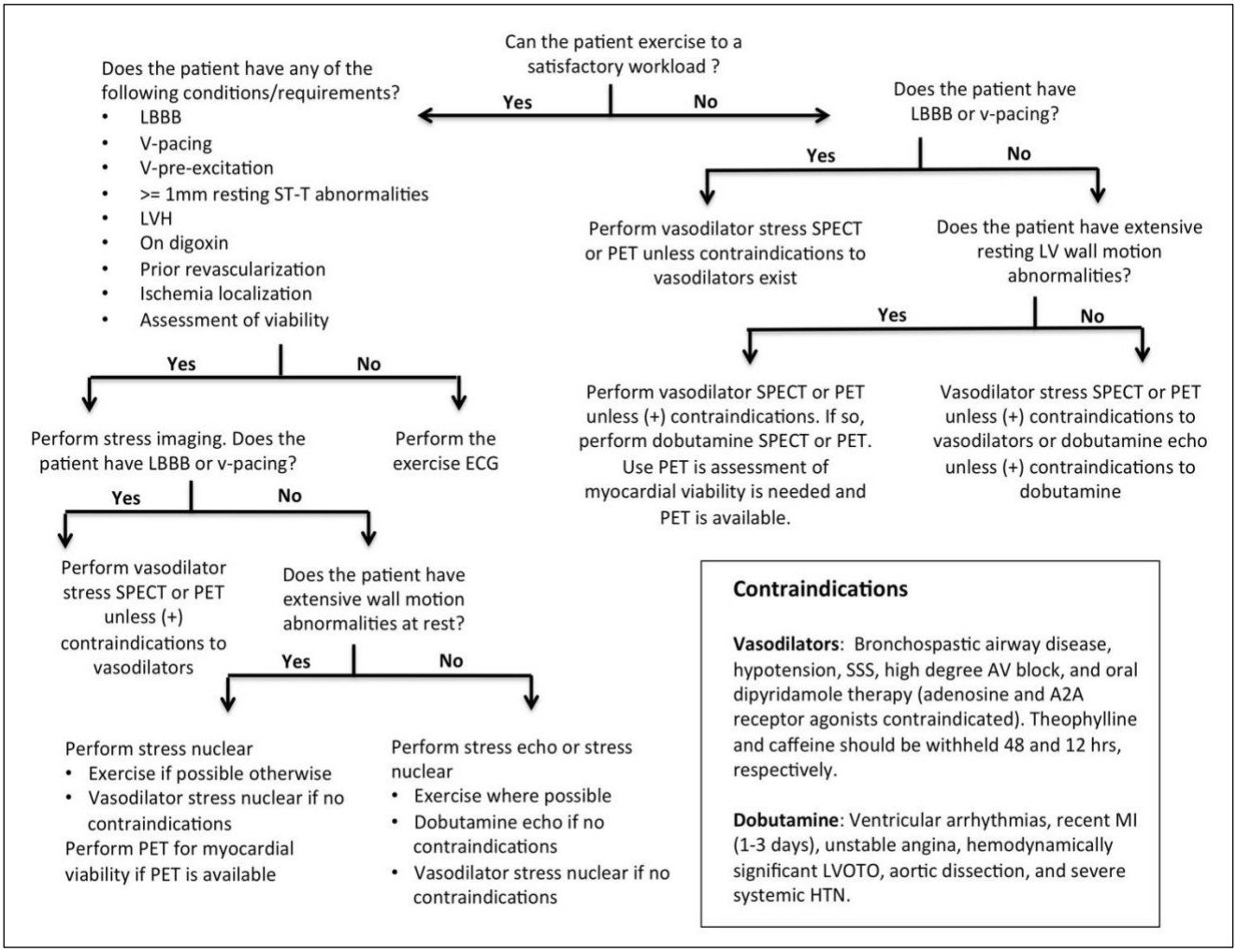
CK-MB: CK-MB peaks within 24 hrs and normalizes within 48-72 hrs. At MGH, CK and CK-MB are no longer used routinely except post-PCI (or post-alcohol septal ablation) to evaluate for infarct size or when reinfarction is suspected.

D. Risk Stratification for non-ACS patients with chest pain: for patients with chest pain who do not meet above criteria for ACS, use HEART score – estimates 6 week risk of MACE score >3 consider for non-invasive or stress imaging

- When compared to TIMI and GRACE, the HEART score was superior at identifying low risk patients, with negative predictive value > 98% for MACE with 1 single troponin (Int J Cariol 2017;227:656)

E. Non-invasive Testing

Schematic Approach to Noninvasive Cardiac Testing (adapted from UpToDate)



Stress testing

- **Indications**:
  - Diagnose CAD: sx of stable angina in pts with intermediate-high risk of CAD. Not indicated for low risk or asymptomatic pts
  - Evaluate new or changing sx concerning ischemia in pts with known CAD
  - Post-revascularization: evaluate pts with ongoing/recurrent angina or asymptomatic pt if incomplete revasc
  - Pre-op risk assessment: not routinely indicated (see *Perioperative Medicine*)
  - Newly diagnosed HF or cardiomyopathy likely due to ischemia, functional capacity (for exercise prescription), viability testing, valvular disorders
- **Contraindications**: **untreated ACS**, MI within 2d, high risk or LM CAD, uncontrolled arrhythmia, acute CHF, recent DVT/PE, acute myo-/peri-/endocarditis, aortic dissection, uncontrolled HTN
- **Preparation**: NPO 3h prior, longer if imaging or adenosine. Must reverse DNR/DNI for test. Hold caffeine >12h for adenosine, > 24h for dobutamine.
  - "*Does the patient have CAD?*" → **hold BB and nitrates**
  - "*How well are meds working in known CAD?*" → **continue BB and nitrates**
- **Caveats**:
  - Majority of vulnerable plaques are angiographically insignificant (<70% stenosis) → stress testing unable to identify the presence of these plaques (CTA more sensitive). CTA may be helpful to rule-out LM disease.
  - Angiographically significant (>70% stenosis) 3 vessel disease may produce false-negative vasodilator stress test → "**balanced ischemia**"
- **Positive test results**: optimize medical tx. Decision re: angiography/revascularization varies by pt.
  - ISCHEMIA trial: revascularization did not decrease ischemic CV events for pts with stable CAD (NEJM 2020;382:1395)

a. Exercise Tolerance Test (ETT) □ *Stress = exercise, Imaging = EKG, SPECT, TTE*
- **i.** ETT preferred over pharmacologic testing if pt is able to reach goal exertion (Bruce protocol or modified Bruce)
- ii. Assesses exercise duration, METs, BP/HR response, HR recovery, double product (HR x SBP)
- iii. **Diagnostic**: >85% max-predict HR (220-age), peak double product (HRxBP) >20k, HR recovery (HR_{peak} – $HR_{1min\ post\text{-}exercise}$) >12
- iv. Increased probability of **ischemia**: □ # of leads with STD, □ degree of max STD, □ METs when EKG changes occur, ventricular ectopy during recovery, increased time to recovery of EKG, failure of SBP to rise with exercise

b. **Pharmacologic Stress Test** □ *Stress = pharmacologic, Imaging = TTE, SPECT, PET, or MRI*
- i. **Choosing an agent**:
  1. **Adenosine/Regadenoson** (act via cAMP): stenosed coronary arteries are already maximally dilated, so flow is "stolen" by healthy vessels ("coronary steal") □ relative perfusion deficit
     a. Side effects: **wheezing, bradycardia, HoTN**. *Caution* if ACTIVE bronchospasm, high grade AVB, SSS, severe AS
     b. Regadenoson: decreased respiratory/conduction side effects, more cost-effective in obese pts. *Caution* if seizure hx (reversal agent aminophylline □ seizure risk)
  2. **Dobutamine**: workload induced by positive inotropy and chronotropy via β-1 receptor agonism
     a. Extremely high dose of dobutamine is given, dose titrated up to 40 mcg/kg/min
     b. Side effects: tachyarrhythmias. *Caution* if MI<48h, hx of malignant arrhythmia, severe AS, HOCM, severe HTN, severe PAH, aortic dissection

c. **Choosing an imaging modality**:
- i. **Nuclear imaging**: utilizes a radioactive tracer to detect areas of □ perfusion between rest and stress states. More expensive than TTE and high amount of radiation (SPECT > PET).
- ii. **PET (**92.6% Sn/ 81.3% Sp) is more sensitive and specific than SPECT (88.3% Sn/ 75.8% Sp) with faster image acquisition. Less widely available and most expensive. Additional uses for imaging in rheumatologic (i.e. cardiac sarcoid) and oncologic contexts (i.e. cardiac myxoma, metastases)
- iii. **TTE**: Reasonable test characteristics to exclude CAD (76% Sn / 88% Sp). May be helpful for hemodynamics/valve disorders.
  1. *Do not use* in pts with LBBB, V-pacing or extensive wall motion abnormalities at rest.

Viability Testing
- Up to 20-40% of patients with CAD and LV dysfunction may demonstrate improved function after revascularization. This is thought to be due to viable myocardium that lacks adequate perfusion ("stunned/hibernating myocardium"). In contrast, necrotic myocardium is unlikely to benefit from reperfusion. Does not require stressor.
- Indication: determine viability of ischemic myocardial tissue ("hibernating myocardium").
- Use is controversial since myocardial viability testing did not identify pts w/ a different survival benefit from CABG compared with medical therapy alone (STITCH trial). Some argue that may have been due to type of viability study used (i.e. SPECT)
  - Imaging modalities: FDG PET, dobutamine TTE, cMRI

Rest Imaging

- **Coronary CTA**: used to evaluate for presence and extent of CAD (JACC 2010;55:2663).
  - Unlike stress imaging, CCTA is an anatomic assessment, *not a* functional assessment.
  - **CT-Fractional flow reserve (FFR)**. FFR is most validated as an invasive assessment during coronary angiography. It can be computed on CCTA to determine the hemodynamic relevance of stenosis. FFR derived from CCTAs closely mimic invasive FFR and may provide some functional data; however, data are limited and there remain limitations (e.g. ostial lesions)
  - Requires cardiac gating (goal HR 60-70, may need to give BB) and respiratory gating (breath hold for 5+ sec) and vasodilators (nitroglycerin)
  - Indications:
    - **Low to intermediate risk patients** in the ED **who present with new CP (i.e. to rule out ACS)**
      - Low risk pts: has high NPV (99%) for CAD rule-out (JACC 2008;52:1724)
      - Moderate risk pts: reasonable for further risk stratification in pts at intermediate risk of CAD or pts with equivocal stress test results
    - Others: Assess patency of CABG, assess for anatomical abnormalities (e.g. course of anomalous coronaries), CTO planning
  - Findings: 2 yr. ACS risk significantly elevated if high-risk plaque (16%) and/or stenotic disease (6%) (JACC 2015;28:337)
    - Higher sensitivity and specificity for coronary stenosis compared to cMRI (Annals 2010;152:167)
  - Limitations: calcified coronaries, prior stents ("blooming artifacts")

- **Coronary Artery Calcium (CAC) Scans:** CT modality that provides risk assessment score (CAC or "Agatston" Score) for coronary artery disease. Either performed alone or concurrently with coronary CTA. Non-gated, non-contrast chest CT scans can be used to provide a qualitative estimation of CAC (Agatston score).
  - Indications: To guide in decision making for primary prevention for asymptomatic adults ≥40 years of age at intermediate risk (7.5 to 19.9 percent 10-year ASCVD risk) if statin therapy decision remains uncertain.
  - Do not use: stand-alone test in evaluation of symptoms of myocardial ischemia, other high risk atherosclerosis patients e.g. familial hypercholesterolemia.
  - Findings:
  - Agatston scores ≥100 or >75 percentile for age and gender independent of ASCVD risk lifestyle changes, risk factor modification (BP, smoking DM tx), and statin therapy. (JACC 2019;73:285)
  - For those with calcium score of 0, reasonable to defer statin therapy for up to 5 years (Circ 2019; 140:496)

Management

A. Myocardial Injury Without Ischemia

- Evaluate for non-ACS causes of elevated troponin (UpToDate)

B. Stable Ischemic Heart Disease

Anti-Anginal Therapy

- Beta-blockers: 1st line therapy to reduce anginal episodes and improved exercise intolerance.
  - Relieve anginal symptoms by decreasing O2-demand (reduce HR and contractility)
  - All beta-blockers are effective.
    - Atenolol may not be cleared in renal dysfunction. May cause less fatigue.
    - Metoprolol XL should be at least BID
  - Improve survival in patients who have had MI or impaired LV (in HF, metoprolol XL, bisoprolol, or carvedilol are only indicated BB)
- CCB: Add-on therapy to BB if ongoing ischemic symptoms
  - Causes coronary artery dilation, reduces contractility
  - Diltiazem, verapamil, or amlodipine are preferred
  - Short acting dihydropyridines (nifedipine) should be avoided unless using with a long acting BB due to the increase in mortality seen in patients after MI or increase in MI in those treated for hypertension
- Nitrates: SL nitro should be provided for patient for acute episodes. Long-acting nitrate can be added to daily regimen.
- Ranolazine: Additional anti-anginal add-on therapy
  - Inhibits late sodium channel (which frequently fails to inactivate in many myocardial diseases and results in disturbances of ion homeostasis)
  - Initial dose is 500 mg BID but can be increased to 1000 mg BID
  - Effective but expensive

Preventative therapy: ASA, statin, ACE/ARB (HTN, DM, HFrEF, CKD), CVD risk factor reduction, flu shot

PCI/CABG:

- Elective for refractory or severe symptoms, change in symptom severity, high-risk coronary anatomy, LV dysfunction (PCI or CABG as appropriate)
- *Mortality*: No convincing evidence [ISCHEMIA trial (NEJM 2020;382), COURAGE trial NEJM 2007;356] that revascularization improves mortality in patients with SIHD as defined by study
  - *ISCHEMIA excluded*: LVEF <35%, LM > 50%, "unacceptable angina," recent onset CCS III angina/progressive angina/CCS IV angina, ACS within 2 months, PCI within 12 months, NYHA III-IV, recent stroke, ESRD, valvular disease, many prior CABG patients.
- *Symptoms*: For patients w/o adequate control of anginal symptoms with optimal medical therapy PCI and CABG have been shown to improve symptoms in two trials MASS II (J Am Coll Cardiol 2004;43) and ISCHMIA (NEJM 2020%3B 382). The ORBITA trial (Lancet 2018;391) shows no benefit in anginal symptoms with PCI, but has been highly criticized.

C. ACS (UA/NSTEMI/STEMI)

Pharmacologic Management: All pts (*w/o contraindications*) should immediately receive the following:

1) ASA 325 mg, chewed/crushed
2) Atorvastatin 80 mg
3) Heparin (ACS protocol)
4) Nitroglycerin – careful in patients with low-normal SBP + large RCA MI

*Decisions regarding P2Y12 inhibitors and other medications should be had in conjunction with cardiology.

Coronary Angiography: All pts w/ ACS should undergo angiography during hospitalization - Optimize medical therapy (see **ACS – PHARMACOLOGIC MANAGEMENT**), **PCI (see section)**, or **CABG (see section)**.

- **Directly to Cath Lab:**
  - STEMI
  - UA/NSTEMI accompanied by high-risk feature: Cardiogenic shock, refractory CP, electrical instability (frequent NSVT, unstable SVT, or sustained VT)
- If the patient has UA/NSTEMI that does not meet criteria for immediate coronary angiography, risk stratify.
  - TIMI (JAMA 2000;284:835) and GRACE (BMJ 2006;333:1091) At MGH, the TIMI Risk Score is most often used.

- TIMI Score of ≥3 or GRACE score of >140 and high clinical suspicion for a Type 1 MI warrants an early invasive strategy (catheterization ≤ 48hrs), though notably, the TIMCAS NEJM 2009;360 study showed that early intervention (≤24 hrs) did not differ from delayed intervention (>36 hrs) in preventing death, MI, or stroke in NSTEMI patients

ACS – pharmacologic management

A. Anti-Platelet

ASA

- Indication: All patients with suspected ACS
- Dose: 325 mg x1, non-enteric coated, chewed/crushed (onset of action 20 min) → 81 mg qD thereafter for lifetime
- MOA: Irreversibly inhibits prostaglandin H synthase (cyclooxygenase-1) in platelets; prevents the formation of thromboxane A2, a potent vasoconstrictor and platelet aggregator.
- Benefit: Mortality reduction and 50% RR non-fatal reinfarction
- Aspirin allergy: Consider substituting a P2Y12 inhibitor. Less common options: cilostazol, or vorapaxar
    - In all cases, ASA desensitization with Allergy/Immunology is recommended when pt stable

P2Y12 Inhibitors

- Indication: STEMI, Type I NSTEMI/UA (regardless of if medical management or an invasive strategy is chosen)
- MOA: Inhibit the G-protein couple receptor P2Y12 that interact with ADP in the process of platelet activation
- Timing: institution-dependent, could delay possible CABG (7 day wash out)
    - *No significant benefit to pre-loading. Do not start in ACS without cardiology*
- Minimum duration (shorter duration associated with worse outcomes - SMART-DATE)
    - BMS: DAPT should be continued for at least 1 month (preferably 1 year)
    - DES: DAPT should be continued for **at least 12 months in patients who underwent PCI for ACS** and **6-12 months for patients who underwent PCI for stable ischemic heart disease**
    - Medical management: at least 1 year
    - Post-fibrinolysis: 1 year
    - Shorter DAPT durations may be safe in specific circumstances (TWILIGHT, STOPDAPT-2, ONYX ONE)
- Prasugrel (TRITON-TIMI38) or ticagrelor (PLATO) preferred over clopidogrel in ACS. Clopidogrel preferring patients with high-bleeding risk.
- Continuing DAPT beyond 1 year: Continuation of clopidogrel for longer may be reasonable (Class IIb, LOE A) in pts who have tolerated minimum course of DAPT w/o a bleeding complication and who are not a high bleeding risk.
    - DAPT Trial: continued DAPT reduced rates of stent thrombosis & MACE, but inc rate of mod/severe bleeding.
    - PEGASUS-TIMI 54: In patients with MI in the prior 1-3 years, an extended regimen of ticagrelor plus ASA significantly reduced the risk of CV death, MI
    - Can use DAPT score to predict combined ischemic & bleeding risk and guide decision making on continuation past 6-12 months (http://tools.acc.org/DAPTriskapp/#!/content/calculator/)
    - No data to continue DAPT beyond 36 months
- Continuing DAPT less than 1-3 months: pts receiving specific types of DES, high-risk bleeding, check with cardiology
- **ACS discharges**: always send 1 year of P2Y12 to pharmacy prior to d/c to ensure supply + check coverage

Clopidogrel:

- Dose: 300-600 mg loading dose + 75mg daily
    - 600 mg dose vs 300 mg dose: Maximal platelet inhibition is reached within 2 hrs w/ a 600 mg loading dose vs. 15-24h w/ a 300 mg loading dose. This correlates with better outcomes both in those with STEMI (HORIZONS-AMI, CURRENT-OASIS) and NSTE-ACS (ARMYDA 2) who underwent PCI
- Benefit: Decrease in the primary end point of CV death, non-fatal MI, stroke (PCI-CURE, PCI-CLARITY)
- Important considerations:
    - **CYP2C19 genotype variants:** poor metabolizers of clopidogrel with decreased response based on high platelet reactivity (unclear relationship to CV events and bleeding). These individuals are at higher risk of in-stent thrombosis with clopidogrel. Switch to another agent.
        - Consider genetic testing if patient presents for in-stent thrombosis.
    - Generic, much less expensive than other anti-platelet choices; remains the treatment of choice for many

Ticagrelor:

- Dose: 180 mg load + 90 mg BID maintenance
- Pharmacokinetics: Reversible binding (faster acting), shorter duration, BID dosing. Does not require activation by CYP450 system
- Evidence/Benefit: Compared to clopidogrel: improves primary end point of MI, stroke, vascular death w/o significant increase in non-CABG related bleeding; reduces in stent thrombosis (PLATO)

  - Consider in ACS/post-PCI
  - Consider in those individuals who have had in stent thrombosis on clopidogrel ("non-responders")
- Important considerations:
  - Side effects: Associated with the development of dyspnea and more rarely, heart block, potentially related to inhibition of adenosine metabolism. Higher bleeding risk than clopidogrel.
  - After 12m, consider ticagrelor 60mg BID for maintenance (or clopidogrel 75mg daily) (PEGASUS-TIMI54)

Prasugrel:
- Dose: 60mg loading dose, followed by 10mg daily
- Pharmacokinetics: Prodrug with more potent inhibitor of platelet aggregation than clopidogrel
- Evidence/Benefit: Reduction in CV death, MI, stroke compared to clopidogrel but high major and life-threatening bleeding (TRITON-TIMI 38). No significant differences in outcomes compared to ticagrelor (PRAGUE-18
- Important considerations:
  - Contraindicated if prior TIA/CVA, weight < 60 kg, or >75 years old
  - No role in pre-cath lab management, or long-term medical management

Cangrelor:
- Dose: 30 mcg/kg bolus followed by 4 mcg/min/kg for PCI
- Pharmacokinetics: **Intravenous**; short half-life (3-5 min)
- Evidence/Benefit: More effective in patients prior to undergoing urgent or elective PCI than clopidogrel in reducing death, MI, and ischemia-driven revascularization at 48 hours; also, less in-stent thrombosis compared to clopidogrel; similar rates of severe bleeding (CHAMPION-PHEONIX)
- Important considerations: May be used in pts awaiting CABG versus high-risk PCI eval. Dosing: 0.75 mcg/kg/min) (BRIDGE)

Switching between P2Y12 inhibitors: Either for cost or bleeding risk (de-escalation, switching to clopidogrel) or need to switch to a more potent agent (escalation, switching to ticagrelor), switching between P2Y12 is sometimes necessary. The most common switches are:
- Switching from ticagrelor to clopidogrel: 24 hours after ticagrelor dose, start clopidogrel load
- Switching from clopidogrel to ticagrelor:
  - Acute/early phase (<30 days): 180 mg ticagrelor irrespective of when the last clopidogrel dose was, ticagrelor maintenance dose given ~24 hours after last clopidogrel dose.
  - >30 days: 90 mg ticagrelor 24 hours after maintenance dose

Glycoprotein IIb/IIIa inhibitors
- Indication: Most commonly initiated in the cath lab and may be continued for 12–24 hours after PCI, especially in those with persistent thrombus. Can be used in NSTEMI with concern for ongoing ischemia awaiting coronary angiography or as (cheaper) bridge to urgent CABG. Usually not needed in patients who have received DAPT and no evidence of ongoing ischemia.
- Drugs: Eptifibatide, abciximab (no longer avail in US), and tirofiban. Eptifibatide (Integrilin) most often used at MGH.
- MOA: Block the glycoprotein IIb/IIIa receptor, the binding site for fibrinogen, von Willebrand factor and other ligands critical to platelet aggregation. Inhibition of this final common receptor reversibly blocks platelet aggregation and prevents thrombosis.
- Evidence/Benefit: Mortality benefit in patients presenting with STEMI not treated with P2Y12 inhibitors. A meta-analysis of 11 trials showed that apiciximab lowered rate of death at 30 days (JAMA 2005;293(14)). Lack of benefit when used with P2Y12 inhibitors w/ increased risk of bleeding (NEJM 2009;360(21))

B. Lipid Lowering Therapy
Statins
- Indication: All patients who present with ACS
- Dose: High intensity statin – Atorvastatin 80 mg or Rosuvastatin 40 mg PO ⍰ Target LDL < 70 mg/dL
- MOA: 1) LDL-C lowering through hepatic upregulation of LDL receptors secondary to inhibition of cholesterol biosynthesis, 2) plaque stabilization and prevention of plaque rupture, 3) anti-inflammatory, anti-thrombotic and endothelial stabilization effects
- Evidence/Benefit: Benefit of high intensity statin (vs prava) seen as early as 15 days post MI (PROVE-IT TIMI 22). Associated with reductions in death, adverse cardiac events, readmission for recurrent angina, atherosclerosis, and reduction in infarct size (MIRACL, REVERSAL)

Ezetimibe
- Indication: patients with MI who have an LDL >70 despite high dose statin
- Dose: 10 mg daily

- MOA: LDL-C lowering through inhibition of an intestinal enterocyte cholesterol transporter thus reducing dietary cholesterol uptake and ultimately promoting hepatic LDL uptake
- Evidence/Benefit: In patients with recent ACS (prior 10d), addition of ezetimibe to a moderate intensity statin is associated with a reduction in CV mortality, major CV event or non-fatal stroke when compared to statin therapy alone. No reduction in all-cause mortality or stroke. *Of note, patients already on a high-potency statin were excluded* (IMPROVE-IT).

PCSK-9 inhibitors (evolocumab, alirocumab)
- Indication: consider if LDL remains > 70 mg/dL on statin + ezetimibe
- Dose: evolocumab 140 mg subq every 2 weeks or 420 mg subq monthly; alirocumab 75 mg subq every 2 weeks
- MOA: PCSK9 binds LDL-R on surface of hepatocytes leading to degradation of LDL-R and higher levels of plasma LDL. PCSK9 antibodies interfere with binding of PCSK9 to LDL-R leading to higher hepatic LDL-R expression and lower plasma LDL levels. Net effect is reduction in LDL-C by as much as 60% in patients on statins.
- Evidence/benefit: FOURIER trial showed reduced risk of cardiovascular death, MI, CBA, stroke, revasc, and unstable angina in patients already on statin therapy with a LDL > 70 (though no decrease in CV mortality or all-cause mortality). ODYSSEY OUTCOMES trial showed reduction composite of death from CAD, nonfatal MI, CVA, unstable angina in patients that had a prior history of MI in 1-12 months prior to enrollment and LDL of at least 70 mg/dL. Also effective as monotherapy (e.g. statin intolerant, GASUS-2, ODYSSEY ALTERNATIVE).

Icosapent Ethyl
- Indication: Consider for use in addition to maximally tolerated statin therapy in patients with triglyceride levels ≥150 mg/dL and either established CVD or T2DM plus ≥ 2 risk factors for cardiovascular disease
- Dose: 2g BID
- MOA: reduction in hepatic production of triglyceride-rich vLDL
- Evidence/benefit: REDUCE-IT (NEJM 2019;380)

C. Beta Blockers
- Indication: Initiated within 24 hours of STEMI/NSTEMI in patients without contraindication reduce the magnitude of infarction, rate of reinfarction, and frequency of life-threatening ventricular tachyarrhythmias
- Dose/Route: Start with metoprolol tartrate 6.25mg PO q6h and titrate up for goal HR 55–60.
    - IV beta blockers should not be routinely given to patients with NSTEMI due to inc risk of cardiogenic shock, though can consider for HTN mgmt if no contraindication (COMMIT)
- MOA: Reduce the magnitude of infarction, rate of reinfarction, and frequency of life-threatening ventricular tachyarrhythmias by decreasing myocardial oxygen demand and sympathetic tone. This occurs by decreasing heart rate, systemic arterial pressure, and myocardial contractility. In addition, prolongation of diastole secondary to the reduction in heart rate may augment perfusion to ischemic myocardium, particularly to the sub endocardium.
- Evidence/Benefit: No RCTs in STEMI pts post-PCI. Studied in STEMI pts and under certain revascularization approaches:
    - No reperfusion: 25% reduction in mortality at 1 year (however, pts did not receive statin or P2Y12 therapy)
    - Fibrinolysis: No high-quality evidence
    - PCI: Conflicting data. One observational study showed significant mortality benefit (JACC 2014;7(6)), others have not (Am J Cardiol 2015;115(11))
- Contraindications (CI): Signs of HF. Relative CI: asthma/reactive airways, PR > 240ms, 2nd or 3rd degree heart block

D. Nitroglycerin
- Indication: Ongoing ischemic discomfort.
    - IV nitroglycerin is indicated within the first 48 hours after NSTEMI for relief of ongoing ischemic discomfort, control of hypertension, or management of pulmonary congestion.
    - IV nitroglycerin should not preclude other mortality-reducing interventions, such as beta-blockers and/or ACEI. Symptom reduction, not mortality benefit.
- Dose: Sublingual 0.4 mg q5m x3 dose; assess for need of IV if ongoing CP
- MOA: Induces smooth relaxation and vasodilation in peripheral veins and arteries reduces cardiac oxygen demand by decreasing preload, with modest effects on afterload and dilation of coronary arteries
- Contraindications: SBP < 90 or ≥ 30 mm Hg below baseline, suspected RV infarction (V4R elevation), or patients who have received a PDE-5 inhibitor (e.g. sildenafil, tadalafil) within 24h
- Side effect: headache, may limit IV titration

E. ACE-I and ARBs
- Indication: within first 24h of (N)STEMI to patients with any of the following: Anterior MI, DM, LVEF < 40%

- Dose/Agent: Can start with short-acting captopril for titration and convert long-acting agent prior to discharge. ARBs with fewer side-effects
- MOA: Attenuate the remodeling of the myocardium, preservation of ischemic preconditioning, reduction of recurrent MI and ischemia (through reducing afterload and mitigating vasoconstriction induced by angiotensin II) and reduction in sudden cardiac death through decreased sympathetic activity and reduced ventricular remodeling
- Evidence/Benefit: ISIS-4, CONSENSUS-II, AIRE, SAVE
- Contraindications: Hypotension (SBP < 100 mm Hg or > 30 mm Hg below baseline)

F. Anticoagulation

- Indication: IV anticoagulation for all patients with NSTEMI/STEMI without contraindication.
- Agent/Dose:
    - Heparin: Unfractionated heparin (at a dose of 60 U/kg bolus followed by 12 U/kg/hr drip, titrating to goal PTT 50–70) is the anticoagulant of choice, especially if the patient will proceed to catheterization as the activated clotting time (ACT) can be followed during the procedure, leading to lower bleeding rates
    - Bivalirudin, Argatroban: Reserved for patients with HIT
    - Enoxaparin: Dose is 1 mg/kg BID. For patients in whom a conservative strategy is selected, Class IIa recommendation to select enoxaparin or fondaparinux over UFH. This is based on evidence of decrease in primary composite end-points as compared to heparin (ESSENCE, TIMI11B, and Phase A to Z trials). Of note, enoxaparin resulted in higher rates of bleeding in patients age > 75 years, though the rate of bleeding was greatest when patients were transitioned from LMWH to UFH or vice versa (SYNERGY). Prefer last dose 8h prior to coronary angiography and possible PCI.
- If on existing oral AC: if warfarin, do not start until INR < 2; if DOAC, consult with pharmacy.
- MOA: Treat/stabilize intra-coronary thrombus and thrombogenesis that leads to acute reduction in blood flow
- Length of therapy:
    - After PCI: Stop unless pt has another indication for anticoagulation (see triple therapy below)
    - Medical management: If PCI is *not* performed (but CAD seen on angiography), can consider continuing:
        - Intravenous UFH for at least 48 hours or until discharge; or
        - Enoxaparin or fondaparinux for duration of the hospitalization, up to 8 days; or
        - Bivalirudin 0.25 mg/kg per hour for up to 72 hours
    - **Heparin rebound syndrome**: D/C'ing UFH results in a brief period of hypercoagulability during which patients may experience worsening angina (NEJM 1992;327(3))
        - Managed through the use of ASA or progressive weaning of UFH drip
        - In patients who cannot receive ASA, another antiplatelet should be utilized consider UFH wean
- Triple Therapy: Ongoing concurrent DAPT and oral anticoagulant therapy increase the risk of bleeding with no significant difference in MI, cardiac death, thrombotic events (WOEST, ISAR-TRIPLE)
    - MGH common practice: treat with triple therapy (ASA/clopidogrel/AC) for 1-4w and subsequently discontinue ASA, continuing AC and clopidogrel (preferred over ticagrelor/prasugrel due to increased bleeding risk)
    - DOAC is preferred over warfarin in most patients (reduced bleeding risk, no lab monitoring). The following DOACs have been studied with antiplatelet therapy in atrial fibrillation:
        - Dabigatran 150 mg BID (RE-DUAL)
        - Apixaban 5 mg BID or 2.5 mg BID in pts w/ at least two of the following: age ≥80 years, body weight ≤60 kg, or serum creatinine ≥1.5 mg/dL (AUGUSTUS)
        - Low dose rivaroxaban (15 mg qPM) was studied in PIONEER-AF-PCI RCT trial but was underpowered to exclude increased risk of stroke therefore some still use the suggested 20 mg qPM for stroke prevention
        - Edoxaban 60 mg daily (ENTRUST-AF PCI); however when compared to warfarin + clopidogrel, edoxaban does not reduce bleeding risk.
    - If pt needs triple therapy, give PPI or H2 blocker for GI ppx (PPI may interact with clopidogrel. No clinical impact suggested, but study terminated early. Expert consensus recommendation).
    - Mechanical heart values: DOACs deemed contraindicated due to an association of worse outcomes in this cohort (RE-ALIGN), <10% of pts included in WOEST and ISAR-TRIPLE studies had mechanical heart valves.

G. Oxygen

- Indication: O2 should be used to maintain SaO2 > 90%. Avoid routine use of supplemental O2 in cardiac patients without hypoxemia as it is not beneficial and may be harmful (Circulation 2015;131(24))
- Evidence/Benefit: No difference in rate of all-cause mortality or rehospitalization in 1 year when comparing patients with SaO2 > 90% randomized to supplemental O2 vs ambient air (DETO2X-AMI)

H. Morphine

- Indication: **almost never** CP unresponsive to NG gtt is an indication for urgent intervention. Morphine *can* be used in refractory pain en route to cath.

- MOA**:** Reduction in pain decreases sympathetic activity
- Of note: Delays antiplatelet effect of clopidogrel and attenuates ticagrelor exposure and action (J Am Coll Cardiol 2014;63(7), IMPRESSION). Associated with increased mortality in NSTEMI patients (CRUSADE)

I. Fibrinolysis

- Indication: **STEMI** pts who cannot receive primary PCI w/in 120 mins of first medical contact (Catheter Cardiovasc Interv 2013;82(1)). In **UA/NSTEMI** there is no benefit of fibrinolysis (possible harm).
- Timing: Time from hospital arrival to initiation of fibrinolysis should be < 30 min. Fibrinolysis has not improved outcomes in patients who present > 12 hrs after symptom onset and thus is not recommended for patients who are stable or asymptomatic.
- P2Y12 inhibitors: Patients receiving fibrinolysis benefit from pretreatment with clopidogrel but not GpIIb/IIIa inhibitors. Ticagrelor may be safe with regards to bleeding (TREAT)

Coronary Angiography and Percutaneous Coronary Intervention (PCI)

Coronary Angiography: A minimally invasive procedure performed in the cardiac catheterization ("cath") lab under fluoroscopic guidance in which iodine contrast is injected into the coronary arteries for structural evaluation

Percutaneous Coronary Intervention (PCI): This is when an intervention is performed on the coronary arteries during coronary angiography. This includes **percutaneous transluminal coronary angioplasty** (**PTCA),** in which a balloon-tipped catheter is inflated to open narrow arteries, with or without stent placement.

A. Access

Most commonly transradial (TRA) or transfemoral (TFA) approach

- The RIVAL trial demonstrated that TRA was non-inferior to TFA in terms of death, MI, stroke, and non-CABG related bleeding; in STEMI subset, TRA was associated with a 30-d all-cause mortality benefit[1]
- Strong evidence to suggest ↓ rates of bleeding and ↓ vascular complications with TRA vs TFA
- AHA endorses a "radial-first" strategy for PCI in ACS[2]

Radial Access**:** After catheterization, a clear plastic band (TR Band) with an inflatable pressure pad is secured around the access site. The sheath (catheter through which procedure was performed) is withdrawn and the inflatable pressure band is adjusted to prevent access site bleeding, while allowing sufficient blood flow to transport hemostatic factors to the hand ("patent hemostasis"). There is a specific nursing protocol to deflate and remove the band when hemostasis achieved (at MGH 2h for diagnostic procedure or 4h post-PCI).

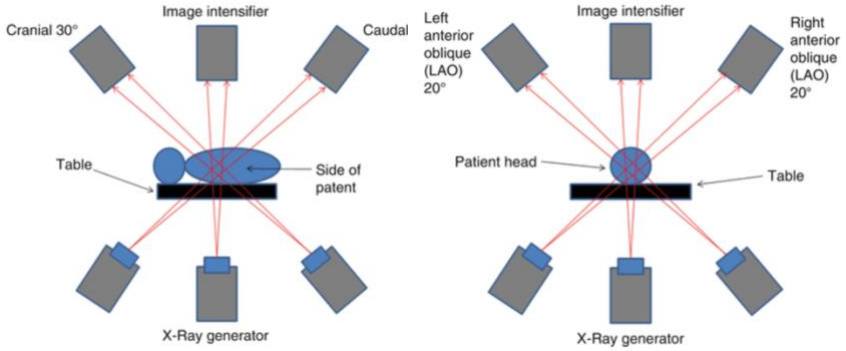
- TR Bands at MGH are managed by the cardiac access fellow, page if any concern for bleeding/expanding hematoma

Femoral Access: After catheterization, the FA sheath can be removed when the activated clotting time is <150-160sec. Manual pressure is applied and the sheath is removed with ongoing pressure for hemostasis (timing determined by size of sheath). Vascular closure devices (e.g. Perclose™ > AngioSeal™) may be used in the Cath Lab in fully anticoagulated patients, patients who have difficulty lying flat and other select scenarios to achieve faster hemostasis. The size of the sheath should be noted post-catheterization as it correlates with bleeding risk.

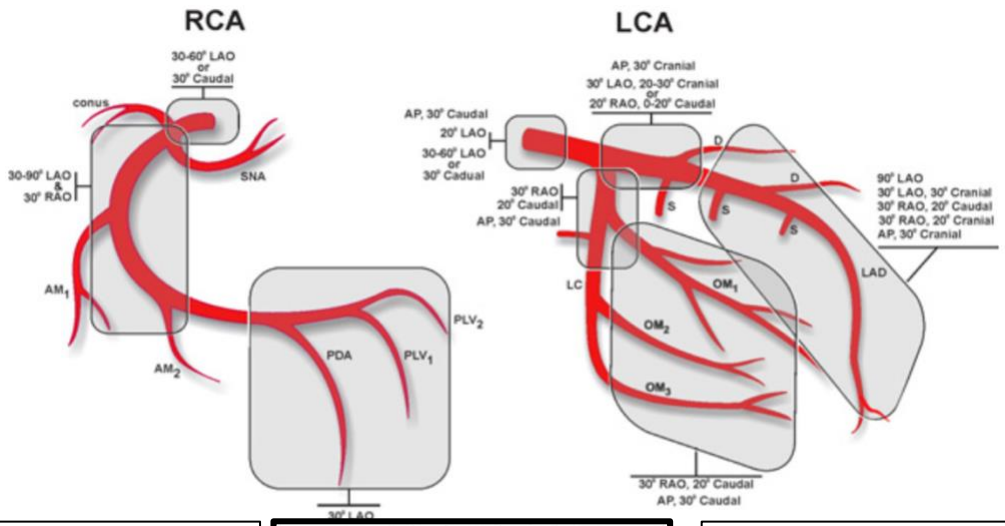
B. Angiographic Nomenclature and Anatomy

In the cath lab, the x-ray source is underneath the table the patient is laying on. The x-ray image is captured by an image intensifier (II) directly above the patient. The body surface of the patient that is closest to the image intensifier determines the specific view.

- Right Anterior Oblique (RAO): II is anterior and on the patient's right-side
- Left Anterior Oblique (LAO): II is anterior to and on the patient's left-side
- Cranial View: II is closest to the pt's head
- Caudal View: II is closest to the pt's feet

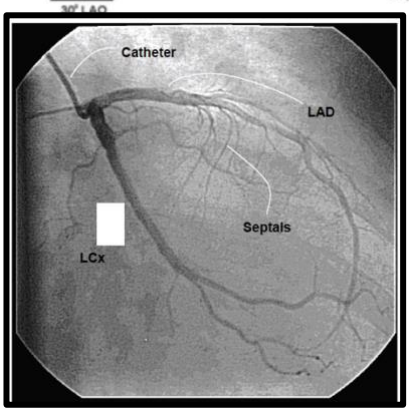


Standard Views

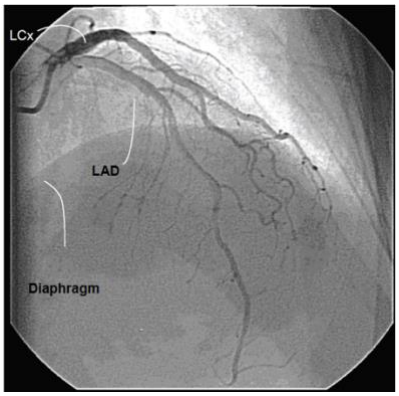


Imaging the LCA:
Left Main (LM): Best viewed with the LAO Caudal ("Spider view") and LAO Cranial
LAD: Best viewed in cranial projections
LCx: Best viewed in caudal projections

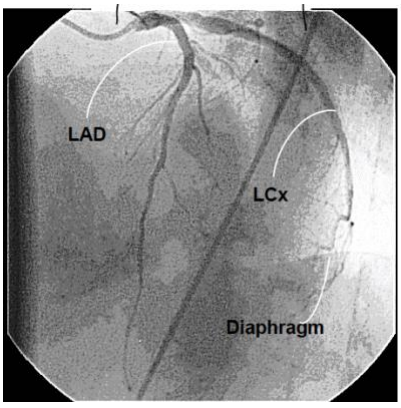
RAO Caudal (LCA): Spine & catheter are on screen left. LCx is clearly delineated. Its branches are named obtuse marginals in numerical order from proximal to distal (OM1, OM2 etc.)



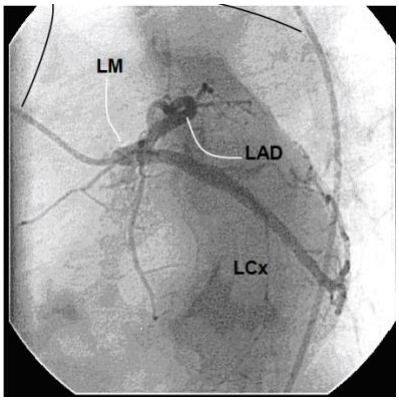
RAO Cranial (LCA): Spine and catheter are on left. Diaphragm is seen. LAD runs anterior to the apex of heart and ends in a shape that resembles "Salvador Dali's mustache." Septal perforators come off the LAD on L, diagonals on R.



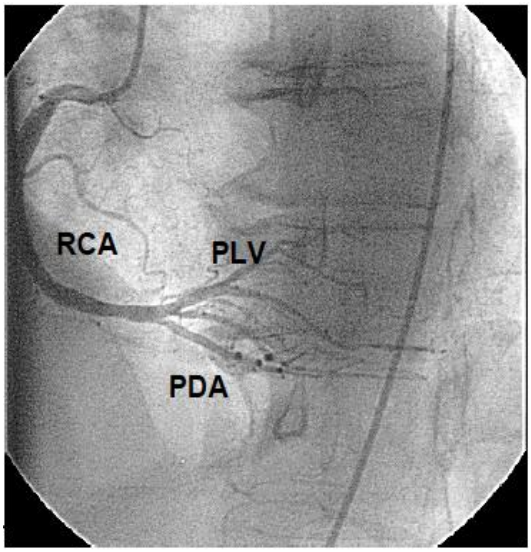
LAO Cranial (LCA): Spine and catheter are on screen right. Diaphragm is seen. LAD and its branches are seen (septal branches and diagonal branches)



LAO Caudal (LCA, Spider View): Spine and catheter are on screen left. LM, proximal LAD and proximal circumflex are in view.



LAO Cranial (RCA): Spine and catheter are screen right. Small branches supplies conduction system. Acute marginal branches (e.g. RV marginal) originate from mid-vessel. Distal RCA branches into the PDA and PLV. The PDA (lowest artery on film), runs in the inferior portion of the interventricular and supplies the posterior portion of the RV, LV and septum. PDA has septal perforators.



C. Identifying Significant Lesions

Fractional Flow Reserve (FFR): ratio of pressures proximal to (aortic pressure) / distal to stenosis (measured by intracoronary wire) at maximal myocardial blood flow ("hyperemia"). Used to evaluate if a stenosis is functionally significant.

- Stable Ischemic Heart Disease: reasonable to use FFR to evaluate functional significance of intermediate-severe coronary stenosis (50-90%). (DEFER, FAME, FAME II)
- ACS: FFR is not used in evaluating culprit lesion, however there is evidence that demonstrates utility in using FFR to revascularize non-culprit lesions in ACS.
    - Stenting of non-infarct related lesions significant by FFR to achieve complete revascularization reduces subsequent revascularization (DANAMI-3-PRIMULTI, Compare-Acute)
- See Fig. 1 for algorithm: https://www.acc.org/latest-in-cardiology/articles/2017/05/25/08/34/ffr-in-2017-current-status-in-pci-management

Instant Wave Free Ratio (iFR): adenosine independent resting-pressure derived index. Non-inferior to FFR (iFR-SWEDEHEART trial)

- Cutoff ≤ 0.89 suggestive of physiologically significant disease and reasonable to consider intervention
- See Fig. 2 for algorithm: https://www.acc.org/latest-in-cardiology/articles/2017/05/25/08/34/ffr-in-2017-current-status-in-pci-management

Intravascular Ultrasound (IVUS): can assist evaluation of left main disease and/or PCI planning (by measuring vessel diameter, lesion length and calcification, as well as confirm stent expansion).

- Use of IVUS supported by meta-analyses suggesting reduced MACE, mortality, and complications with IVUS vs. angiography alone.
- **Optical Coherence Tomography (OCT)** has higher spatial resolution than IVUS but less depth penetration. Data suggest equivalence to IVUS; trials ongoing.

PCI of Non-culprit Lesions

- NSTEMI/UA: Controversial. No RCTs, only observational studies. Most studies support complete revascularization.
- STEMI: There are 4 options in the management of non-culprit lesions in STEMI: 1) no revascularization, 2) PCI at time of primary PCI, 3) Staged PCI either during index hospitalization or post-discharge, 4) CABG in those that have clear indications
    - Evidence that PCI of non-culprit lesions leads to better outcomes (especially need for repeat revascularization): PRAMI, CvLPRIT, DANAMI-3-PRIMULTI. Timing of intervention remains uncertain.
        - 2015 ACC/AHA guideline: IIb recommendation for PCI to non-culprit lesions.
    - May be harmful in STEMI with cardiogenic shock: CULPRIT-SHOCK
- Which non-culprit lesions? Any lesion that looks unstable, stenosis ≥ 70%, use FFR in lesions ≥ 50%. If there is a question regarding viability of the tissue to the area, viability imaging may be reasonable prior to PCI.
- CTO (chronic total occlusion): Optimal management of non-culprit CTO in STEMI is not known. CTO-PCI is primarily indicated for morbidity benefit in patients with refractory angina +/- LVEF recovery. Would defer to outpatient evaluation once optimally medically managed for angina/HF.

D. Aspiration Thrombectomy

2015 ACC/AHA guidelines recommend against aspiration routine thrombectomy in patients undergoing PCI for STEMI. This is based on three large trials (TOTAL, TASTE, TAPAS) and the subsequent meta-analysis, that did not find improved outcomes with this strategy.

E. Stent Placement – Bare Metal Stent (BMS) vs Drug Eluting Stent (DES)

BMS: Consider in pts w/ high bleeding risk, need for invasive procedures, or difficulty with adherence to 1yr DAPT

- More likely to develop early in-stent restenosis due to re-epithelization within the first 30 days
- Requires DAPT for at least 1 month (preferred 1 year)
- With reduction in stent thrombosis in newest generation of DES and short-DAPT regimens in high-bleeding risk individuals, BMS are *rarely* used.

DES: Contain anti-proliferative drug and polymer that serves as vehicle for the drug and controls the rate of release. The drug inhibits the growth of the neointima, which is the major cause of restenosis. Associated with increased rate of late (>30 day) stent thrombosis due to prolonged foreign body exposure

- Requires DAPT for at least 6 months in SIHD (preferred 1 year) so theoretically increases bleeding risk
- The NORSTENT trial comparing 2nd generation DES vs. BMS found no significant difference in mortality, but noted ↓ repeat revascularization in DES group
- Emerging evidence suggests newer generation DES w/ shorter DAPT may be considered (LEADERS FREE II, ZEUS, ONYX-ONE)

Assessment of Blood Flow Before & After Intervention:
- TIMI 0 Flow (no perfusion): Absence of any antegrade flow beyond a coronary occlusion
- TIMI 1 Flow (penetration w/o perfusion): Faint antegrade flow beyond the occlusion, w/ incomplete filling distal to the coronary bed
- TIMI 2 Flow (partial reperfusion): Delayed or sluggish antegrade flow with complete filling of the distal territory
- TIMI 3 Flow: Normal flow fills the distal coronary bed completely

Post-Cath Care

Pass-off Essentials in SDU/CCU:
- Type of access used for procedure (Arterial v Venous, Femoral v Radial v Jugular)
- Sheaths: What sheaths are in place, by whom they should be removed, removed in post-cath holding area vs. if closure device used (relevant for bedrest), for how long should bedrest be?
- Medications in cath lab (ex. Anti-platelet loads)
- Drips (heparin, eptifibatide, cangrelor, etc) and parameters to stop
- Planned course for anti-platelet agents & a/c, especially P2Y12 (P2Y12 ordered prior to transfer by cardiology fellow).
- Findings of procedure and devices/stent details (DES v BMS, size, location)
- Complications of procedure

Post-Cath Orders/Vascular Access Questions:
- Interventional fellow will place some post-cath orders (IVF, AC); always clarify AC with fellow
- Day questions/issues about procedures directed to procedural fellow during day
- Night questions/issues
    - Re: vascular access: Direct to moonlighting fellow on Cardiac Access Unit for interventional procedures (Ellison 11, call floor, ask for fellow) and to EP fellow for EP procedures
    - Other issues are not responsibility of access fellow (ex if patient unstable and needs to return to cath lab, notify daytime cards attending or on-call PDW cards fellow). For STEMI, call 6-8282 to speak with Cath Lab during the day or Interventional Cardiology Attending at night.

Sheaths and Removal:
- When FA sheaths (catheter through which procedure is performed) in place, patients must strictly lie flat (head of bed < 30-degrees), after removal need to remain flat for 4-6hrs (reverse Trendelenburg used if patient needs to sit forward to eat, take meds, or reduce aspiration)
- Arterial sheaths removed by interventional fellow (or Access Fellow on E11 at night) and require at least 20-30min manual pressure
- Vascular closure devices occasionally used to remove sheath despite an elevated PTT (otherwise heparin gtt needs to be off and PTT checked)
- PTT goals vary but achieving near normal PTT ↓ bleeding complications
- SBP goal <140 if possible, to reduce pressure on platelet plug
- If radial access, TR band used for hemostasis there are few activity restrictions (removal is nursing protocol driven)
- Common restrictions: No lifting > 10 lbs x 7 days (with affected hand if radial access); no driving at least 48h post-proc

Vascular Closure Devices (VCD):
- Gold standard is manual compression for hemostasis
- VCDs placed in cath lab to continue AC, shorten bedrest, and reduce manual pressure time
- Most common femoral devices in MGH lab: Angio-seal (endovascular pad with extravascular collagen plug), PerClose (uses sutures), StarClose (extravascular clip)
- TR band used for radial access, removal on floor/unit per nursing protocol

Access Site Complications
- Hematoma: more common w/ femoral access.
    - **Apply pressure (arteriotomy site is 2 fingerbreadths proximal to skin puncture).** Fem-O-Stop device can be used to apply constant pressure if uncontrolled bleeding or unable to interrupt anti-platelets (carefully monitor distal perfusion with help of fellow); *only when advised by procedural fellow/attending.*
    - IVFs, control blood pressure, and consider reversing AC (after discussing with attending
- Retroperitoneal Bleed: may present with HD instability, ipsilateral flank pain and ecchymosis; up to 20% mortality • Risk ↑ in females with very low or high BMIs.
    - Assume that any hypotension post-procedure is RP bleed (especially with femoral arterial access is)
    - Management includes immediately notifying attending, large bore IV access, IVFs, blood products, and consider stopping/reversal of antiplatelet/anticoagulant agents
    - Only proceed to non-contrast CT if patient is stable. Otherwise, defer and treat as if were RP bleed
- Limb ischemia: due to thrombus, dissection or complication of closure device
    - Be sure to exam access sites (pulse, bruit) and distal pulses (Doppler PRN) PRIOR to procedure for comparison post-procedure
    - Evaluate distal pulses with Doppler and consider PVRs to further assess location of compromise

Cardiopulmonary Bypass Grafting (CABG)

A. Indications for CABG

Class I: Significant (>50%) L Main Disease or equivalent (>70% prox LAD + prox LCX), 3VD, Significant (proximal, long) LAD Disease with 1-2VD and EF<50%, 1-2VD without LAD involvement but large area of at-risk myocardium
Class IIa: Significant proximal LAD Disease with 1-2VD without high-risk features. PCI may be reasonable.
Class IIb: 1-2VD without LAD and without high-risk features. PCI often preferable.

B. Bypass Grafts

Arterial: Arterial grafts >> long-term survival compared to vein grafts: >90% patency rate at 10 years, ↑ survival, ↓ MI, ↓ less recurrent angina, ↓ reoperations; arterial ↑ grafts difficulty to harvest compared to SVG so may not be used in emergent situations

- Internal Thoracic Arteries (ITA) *[LIMA/RIMA]:* Native take off from the subclavian with end-to-side anastomosis to coronary, limited by vessel length to proximal touchdown on coronaries (for bypassing proximal stenosis)
  - ITA grafts confer 20 yr. survival benefit compared to SVGs alone
  - LIMA anatomically favorable for LAD, so most common graft
  - RIMA technically challenging, increases pump time; can be used in-situ to bypass RCA or OM w/ critical stenosis (>90%) or in Y-graft with LIMA to other target vessels.
  - Prefer to avoid bilateral ITA in poorly controlled diabetics due to concern for sternal wound healing
- Radial Arteries: 80-85% patency at 5yrs; ↑ patency and ↓ adverse cardiac events compared to SVGs[31]
  - Can bypass severe (>70%) L sided stenosis or critical (>90%) R sided stenosis
  - Safe harvest, sometimes numbness/tingling in hand ipsilateral to harvest but generally no motor compromise
- Gastroepiploic Arteries*:* 15 yr. patency rate >92%, rarely used

Venous: SVG 5-7 yr. patency ~50%

- Requires ASA within 48hrs s/p CABG, continued indefinitely
- Smoking, HTN, HLD, DM ↑ risk for graft failure

Key Points:

- Arterial grafts ↑ patency compared to SVGs; may not be limited to RIMA/LIMA with increased radial artery grafting
- Arterial grafts ↑ difficulty to harvest compared to SVGs, so less conducive in emergencies

C. Concomitant Medical Therapy

- ASA 81-325 mg/day (clopidogrel 75mg/day if intolerant/allergic to ASA): Associated w/ decrease in-hospital mortality, MI, stroke, and renal failure in patients who received w/in first 48 hours. Should be continued post-operatively.[32]
- P2Y12 therapy: Controversial and practice-dependent. Some surgeons use if prior stents (esp. if not bypassed) or limited operative outflow from grafts. Subset of the CURE trial suggested a non-significant decrease in CV death, MI, stroke.[33]
- Statin: High intensity statin for all <75 unless drug-drug interaction or intolerance
- Beta-blocker starting peri-operatively to reduce post-operative AF.
  - No difference between BB and amiodarone re: AF at follow-up (Gillinov et al. NEJM 2016;374)
  - 2014 review, there was no mortality benefit in beta blocker seen in patients undergoing CABG without ACS in the past 21 days.[34]
- Anticoag: COMPASS-CABG Study demonstrated that rivaroxaban 2.5mg BID + ASA 100 daily or rivaroxaban 5mg BID vs ASA 100 alone did not reduce graft failure, but rivaroxaban 2.5mg BID + ASA 100 associated with ↓MACE.[35]

D. CABG vs PCI

Syntax Score: Developed for SYNTAX Trial, which randomized patients with 3VD or LMCA to CABG vs PCI

- Syntax Score is a semi-quantitative tool based on coronary angiography that grades anatomic complexity
- ↑ Syntax Score = better outcomes with CABG, while ↓ Syntax Score = non-inferior outcomes compared to PCI
- Multidisciplinary Heart Team meetings at MGH between cardiothoracic surgery, interventional cardiology, and primary team to decide intervention in complex situations

Specific Considerations:

LMCA Disease: Historically CABG was standard for LMCA disease, some recent randomized trials showing PCI with DES may be reasonable for certain patients but the data are mixed (SYNTAX, PRECOMBAT, NOBLE, EXCEL, MAIN-COMPARE)
DM w/ limited overall CAD: No difference in 5yr survival, but rate of MACE was lower in CABG (BARI-2D)
DM w/ advanced CAD: CABG is superior to PCI in the management of patients with DM2 and multivessel disease with respect to prevention of MI and death, although at a cost of a higher risk of stroke (FREEDOM)

CABG + OMT vs. OMT alone in Ischemic Cardiomyopathy: All-cause mortality, cardiovascular mortality and hospitalization for cardiovascular causes were significantly lower in patients who underwent CABG + medical therapy than those who received medical therapy only. Benefit seen over time; at least 5 year-survival **(**STICHES)

Post-MI Complications

Mechanical Complications (JACC 2013;61:e78, JACC 2019;12(18):1825-1836.)

Complication	Prevalence / Risk Factors	Timing / Clinical Signs	Evaluation	Treatment
Early Complications (Hours – Days)				
Cardiogenic Shock (see *Inpatient HF*)	▪ STEMI ~6% ▪ NSTEMI ~3% ▪ Anterior MI, LBBB, prior MI, 3VD, age, HTN, DM, mechanical complications ▪ 50% of post-MI death	▪ STEMI: of pts that develop shock, 50% w/in 6h of MI, 75% w/in 24 h ▪ NSTEMI: 72-96 h after MI ▪ New onset CP, cold/wet physiology, HoTN, tachycardia, dyspnea, JVD, rales (66%), new murmur	▪ TTE ▪ PA catheter (CI<2.2,PCWP>18) ▪ End organ hypo-perfusion (lactic acidosis, AKI)	▪ Inotropes/pressors ▪ Emergent PCI/CABG (<75y + STEMI + shock w/in 36h of MI). SHOCK trial (NEJM 1999;341:625) ▪ IABP and other MCS
Myocardial Free Wall Rupture (Pseudoaneurysm: LV defect contained by only pericardium/ scar, more prone to rupture than true aneurysm)	▪ 0.01% STEMIs & NSTEMIs ▪ Transmural MI, 1-vessel MI, 1st MI (poor collaterals), anterior and lateral MI, HTN, late thrombolysis (>14 h), fibrinolysis>>PCI, NSAIDs, female, age >70 ▪ Accounts for 10% post-MI death	▪ 40% w/in 24h, 85% w/in 1 week ▪ Tamponade in 85% ▪ Olivia's triad: pericarditis, repetitive emesis, restlessness/agitation (PPV 95% w/ 2/3). (JACC 1993;22:720) ▪ Electromechanical dissociation, aberrant T wave evolution, abrupt episodes of ↓HR/BP	▪ TTE (pericardial effusion w/ high acoustic echoes indicating clot) ▪ STAT cardiac surgery consult	▪ Emergent surgery for resection of ruptured myocardium w/ primary reconstruction
Interventricular Septal Rupture (VSD)	▪ 0.21% STEMIs, 0.04% NSTEMIs ▪ 1st MI, 1-vessel MI (esp. LAD), CKD, anterior infarct w/ inferior STE due to wrap-around LAD, older age, female ▪ 5% of post-MI death	▪ Bimodal: 24 h and 3-5 days to up to 2 weeks from event ▪ New, harsh holosystolic murmur (50% w/ thrill), S3, loud P2, hypotension, BiV failure (R>L)	▪ TTE w/ doppler (L to R shunt, RV overload) ▪ RHC: increase in O2 sat from RA to PA >5, large v waves	▪ Emergency surgery or transcatheter closure device ▪ Vasodilators (use cautiously) to decrease L to R shunt (nitroprusside or nitroglycerin) ▪ IABP
Papillary Muscle Rupture (leading to acute MR)	▪ 0.05% STEMIs, 0.01% NSTEMIs ▪ Posteromedial (supplied by PDA, with inf. or post. MI) >> anterolateral (dual blood supply by LAD and LCx) ▪ 5% of post-MI death	▪ No reperfusion: 2-7 d ▪ With reperfusion: median 13h ▪ Abrupt dyspnea, pulmonary edema, hypotension ▪ Hyperdynamic LV, holosystolic murmur at apex (radiates to LSB w/ posterior pap muscle rupture), murmur may be absent in torrential MR or severe HF	▪ TTE (MR) ▪ CXR: edema (can be asymmetric to RUL if MR jet directed at right pulmonary veins) ▪ Tall *c-v* wave in PCWP tracing	▪ Aggressive afterload reduction (nitroprusside or nitroglycerin) ▪ IABP ▪ Emergent surgery

Late Complications (Weeks – Months)				
LV Aneurysm (discrete, dyskinetic area of LV with broad neck, rarely ruptures)	▪ No reperfusion: 10-30% ▪ Apical-anterior wall >> inferior posterior ▪ Steroids, NSAIDs	▪ Days to weeks ▪ Acute: diffuse, displaced PMI, S3 and/or S4, MR murmur, CHF ▪ Chronic: HF, VT/VF, systemic embolization, may be asymptomatic	▪ ECG w/ persistent STE ▪ TTE or other imaging (CMR, CT, ventriculography)	▪ Acute: management of CHF, ACEi, avoid NSAIDs/steroids, start heparin (if EF<35%) ▪ Chronic: ACEi, digoxin, diuretics, warfarin (if EF<35%), Surgical repair
LV Thrombus	▪ 5% of AMI patients post-PCI ▪ Usually in LV apex ▪ Large infarct size, severe apical akinesis or dyskinesis, LV aneurysm, anterior MI	▪ Can form 24-72h post MI ▪ 90% of thrombi are formed by 2 weeks post MI ▪ Embolization risk persists for 6 months but highest in first ~3 months; risk is 10% if not on warfarin	▪ TTE with contrast ▪ CMR or CT	▪ Warfarin (INR 2-3) ▪ When to stop warfarin unclear, check for resolution of thrombus on TTE at 3-6 months
Pericarditis	▪ 5% of pts in the ED w/ CP and no MI, male predominance ▪ 85-90% idiopathic (viral/post viral), infectious, post-MI, uremic, autoimmune, malignancy, XRT, drugs	▪ 10% at 2-4d post-transmural MI ▪ May be focal or diffuse ▪ Dressler's syndrome: malaise/fever, leukocytosis, late autoimmune carditis, rare	▪ ECG (diffuse STE, PR depressions) ▪ TTE (effusion) ▪ CMR and/or cardiac CT (if needed to confirm)	▪ ASA + colchicine ▪ Avoid NSAIDs and steroids post MI as can impair infarct healing
Coronary Artery In-Stent Thrombosis	▪ Highest risk is absence of P2Y12 inhibitor ▪ 1% at 1 year, then ~0.2% per year thereafter	▪ Most cases occur within 30 days of PCI irrespective of stent type ▪ ACS symptomatology	▪ ECG ▪ Biomarkers (troponin/CKMB)	▪ PCI ▪ Long term anti-platelet therapy, adherence to therapy

Electrical Complications:

- Bradyarrhythmia/conduction block: may be due to coronary artery occlusion (see below) or Bezold-Jarisch reflex (Anes 2003;98:1250)
- Tachyarrhythmia: related to creation of re-entrant circuit from scar formation and/or ↑ automaticity from adrenergic

	Arrhythmia	Location/Mechanism	Incidence/Timing	Treatment/Outcome
Bradyarrhythmias	Sinus bradycardia	▪ Inferior and posterior MI ▪ Beneficial:↓myocardial O2 demand	▪ Up to 40% of acute MI ▪ Occurs early in STEMI	▪ Atropine, atrial pacing if unstable, dopamine/epi if hypotensive
	First degree AVB	▪ Inferior: ↑ vagal tone *or* AV node ischemia (RCA), narrow QRS ▪ Anterior: septal necrosis below AV node, RBBB, wide QRS	▪ More common in inferior MI	▪ If due to inferior MI, transient (vagal) ▪ Continue CCB or BB unless PR interval is longer than 240ms.
	Second degree AVB: Mobitz Type I	▪ Usually inferoposterior MI (↑ vagal tone, narrow QRS) or AV node ischemia	▪ Usually within first 24h of MI	▪ Usually transient; observe ▪ Atropine if symptoms or HR < 45
	Second degree AVB: Mobitz Type II	▪ Usually, anterior MI with infranodal conduction injury, wide QRS, HR often < 30, 33% progress to CHB	▪ Usually within first 24h of MI	▪ Consider temporary pacing ▪ In infranodal block, *atropine may paradoxically worsen AV block*
	Third degree AVB	▪ If inferior MI: intra-nodal lesion; narrower QRS escape ▪ If anterior MI: infra-nodal lesion; wide, unstable escape rhythm	▪ 3-7% acute MI ▪ Inferior: gradual, stable ▪ Anterior: sudden, 12-24h after MI	▪ Recovery 3-7 days; temp pacing required ▪ Inferior: transient, resolves on own ▪ Anterior: carries high mortality rate (80%) and indicates extensive necrosis
Intraventricular Conduction Blocks		▪ 50% already present on first ECG, may represent antecedent disease of conduction syndrome ▪ Suggests more extensive infarct	▪ 2-5% of MI	▪ Patients w/ BBB are more likely to have comorbid conditions, less likely to have received therapies, have larger area infarcts, and have high mortality
Supraventricular Arrhythmias	Sinus tachycardia	▪ May be compensatory for LV dysfunction, common in anterior MI ▪ Pain, anxiety, pericarditis, fever	▪ 25% of acute MI	▪ Undesirable as ↑ myocardial oxygen, ↓diastole time causes ↓coronary perfusion time ▪ Treat underlying cause
	Atrial fibrillation/ Atrial flutter	▪ Early: may be transient due to ↑sympathetic; atrial ischemia ▪ Late: due to atrial stretch/HF	▪ 6-8%, may be >30% of acute MI	▪ Associated with mortality, particularly if late (>30d) AF (Circ 2011;123:2094) ▪ If unstable, cardioversion; consider BB, amiodarone, digoxin, anticoagulation

Ventricular Tachyarrhythmias	Premature Ventricular Contraction	▪ Due to electrical instability and increased sympathetic tone	▪ Variable	▪ Correct electrolyte deficits, beta-blocker. Do NOT treat with anti-arrhythmics as can ↑ mortality (NEJM 1991;324:781)
	Accelerated Idioventricular Rhythm (AIVR)	▪ 50-110bpm, higher V- vs. A-rate; in 40%, considered a reperfusion rhythm	▪ Up to 20% of STEMI ▪ Usually within 12-48 h, can occur after reperfusion	▪ Do not treat unless symptomatic or hemodynamically unstable, usually short duration and does not affect prognosis
	Ventricular Tachycardia	▪ Monomorphic VT<170bpm is unusual early after STEMI, suggests pre-existing arrhythmogenic scar; recurrent ischemia usually polymorphic VT	▪ NSVT 1-7%, sustained VT (2-3% of STEMI, <1% NSTEMI) ▪ Usually 48h post STEMI, late VT (>48h) has very poor prognosis	▪ Antiarrhythmic agents (amio, lidocaine) ▪ Urgent resvasc if due to ischemia ▪ Cardioversion/defibrillation to prevent VF and restore hemodynamic stability ▪ Correct underlying abnormalities (pH, K, Mg, hypoxemia)
	Ventricular Fibrillation	▪ Risk factors: ↑ age, prior MI (scar), anterior MI, cardiogenic shock, ↓ LVEF, CKD ▪ VF >48h post-MI may indicate LV dysfunction	▪ 5% of STEMI ▪ 1% of NSTEMI	▪ ACLS/defibrillation ▪ Anti-arrhythmic infusion (24-48h amiodarone post-defibrillation) ▪ Maintain K>4, Mg>2.2

Special Populations

Myocardial Infarction with Non-obstructive Coronary Arteries (MINOCA):

Definition: Rise & fall of troponins with symptoms suggestive of ischemia, but angiogram with non-obstructive disease (≤ 50% stenosis)

Epidemiology: 1-14% in patients presenting with MI
Risk Factors: ~ CAD (DM, HTN), more likely to be younger (mean age=55) and female
Ddx: Coronary spasm, microvascular disease, missed lesion on cath (indeterminate/eccentric plaque, fibrinolysis prior to angiography), SCAD, takotsubo cardiomyopathy, coronary artery embolism, viral myocarditis
Treatment: Depends on etiology. For patients that have some evidence of CAD and no evidence of alternative etiology, reasonable to assume ACS and medically manage with ASA, P2Y12, beta-blocker, and statin
Prognosis: Meta-analysis of 8 studies showed in-hospital mortality of 0.9% with 12-month mortality of 4.7%. Generally, the mortality is lower than in patients with MI with obstructive CAD

Spontaneous Coronary Artery Dissection (SCAD):
Definition: non-traumatic dissection of the coronary arterial wall

Epidemiology: Accounts for 1-4% of all MIs, may account for up to 35% of MIs in women ≤ 50, most common cause of ACS in pregnancy 43%; 1.81 events per 100,000 pregnancies. Average age of women 45-53

Risk Factors: Female gender, pregnancy (usually third trimester, early post-partum), FMD and other arthropathies. Classically associated with physical or emotional stress
Pathophysiology: Creation of a false lumen with intramural hemorrhage either by intimal tear or bleeding of the vasa vasorum. The enlarging hematoma then encroaches on the true lumen causing myocardial ischemia. The LAD is the most commonly effected artery (32-46%). The mid-distal sections are most commonly affected.
Clinical Manifestations: Vast majority present with ACS with STE, 2-5% present in cardiogenic shock
Diagnosis:

- Coronary Angiography (gold standard): angiographic classification due to the different appearances of SCAD on angiography. Coronary angiography carries more risk of iatrogenic coronary artery dissection than in other cases (3.4% vs 0.2%)
- CTA Coronary: Sometimes able to identify SCAD but lower sensitivity than coronary angiography. Often used for follow-up

Treatment:

- Conservative management (no revascularization) generally recommended in patients that are hemodynamically stable without high risk anatomy. Angiographic healing has been shown to occur in patients that had repeat angiography in the weeks to months after (70-97%). Early complications may occur in these patients – 5-10% develop recurrent MI within the first 7 days. These patients commonly need urgent angiography with PCI. Monitor inpatient for 3-5 days for signs and symptoms of ongoing ischemia.
- PCI: Only considered if ongoing ischemia or HDUS. Increased complications in patients with SCAD that underwent PCI due to the risks of complications that occur with stent placement (extension of dissection, etc).
- CABG: Consider if LM, proximal 2-vessel dissection, or if complication of PCI.
- Medical therapy: Lack of consensus w/ wide practice variation; discuss with cards. 2017 AHA Expert Opinion SCAD:
    - Anticoagulation: Once SCAD is diagnosed, reasonable to stop heparin given concern for propagation of intramural hematoma (although could reduce thrombus formation).
    - Anti-platelet: Wide variation in use and recommendations of DAPT. Generally, aspirin is prescribed.
    - Beta-blockers: Should be considered in all patients with low EF or arrhythmias. Low HR decreases shear stress on arteries.
    - Statins: Not recommended routinely after SCAD but is indicated if have concomitant hyperlipidemia.
- Activities after SCAD: patients should be referred to cardiac rehab (SCAD-specific if available). Target HR during exercise should generally not exceed 50-70% of HR reserve and systolic blood pressure should generally be < 130. Avoid lifting heavy weights (W < 20-30 lbs, M < 50 lbs). A dedicated SCAD rehab program was shown to be beneficial in patients (reduced chest pain, improving exercise capacity, and reducing CV events)

Prognosis:

- Pregnancy-related SCAD has worse prognosis than non-pregnancy related SCAD
- In-hospital mortality: 4.2%
- Recurrent in-hospital MI: 4.6%, unplanned revascularization: 4.3%
- At intermediate follow up (2-3 years), recurrent MI reported in 10-30%
- At long term follow up (10 years): MACE in ~50%, most commonly recurrent SCAD

Microvascular Angina
Definition: Symptoms of angina + signs of ischemia on non-invasive testing, but on evaluation of epicardial coronary arteries, no obstructive coronary disease
Epidemiology: More likely to be younger and female, more likely to have CV risk factors than the general population
Clinical Presentation: Some patients present with ACS and then are diagnosed with MINOCA. Others have stable coronary disease that get the diagnosis after persistent and severe symptoms lead to coronary angiography without evidence of obstructive CAD
Pathophysiology: Various mechanisms proposed, but it has been shown that these patients have higher sensitivity to vasoconstrictor stimuli and less ability to vasodilate. Other mechanisms include endothelial dysfunction, luminal obstruction (microthrombi), vascular remodeling, extramural compression, pain sensitivity. Can coincide with other CV conditions, such as HCM, LVH, aortic stenosis due to one of the many mechanisms proposed
Diagnosis: Stress testing, PET-stress in particular can assess coronary flow reserve/microvascular disease. Coronary angiography +/- provocative testing.
During angiography:

- Coronary Flow Reserve (CFR): More commonly measured by PET-stress. Can administer intra-coronary vasodilator and measure the flow reserve during coronary angiography. If the CFR is low (<2-2.5) and there is no epicardial disease, microvascular dysfunction can be diagnosed
- Provocative testing with Ach: diagnostic if have symptoms + EKG changes without evidence of epicardial disease

Non-invasive

- Fractional flow reserve using CT, PET, or CMR

Treatment:

- Risk factor modification
- Aspirin and statin if have any evidence of atherosclerotic disease
- Anti-anginal: as listed in SIHD
- ACE-I: There is some evidence of benefit. For example, in the WISE trial, women who had received quinapril had improved CFR after 16 weeks. They also had improved symptoms of angina
- Imipramine: Small study showed 50% reduction in chest pain

Cocaine-induced myocardial infarction
Treatment:

- ASA 325 mg unless suspicion of acute aortic dissection
- Sublingual nitroglycerin 0.3-0.4 mg q5min until chest pain is relieved up to 3 doses
- Calcium channel blockers are adjunctive treatments for ongoing/recurrent symptoms of ischemia despite optimal therapy with nitroglycerin. Usually IV diltiazem 5-20 mg or verapamil 2.5-5 mg is used
- For agitation 2/2 cocaine, benzodiazepines (diazepam 5-10 mg IV q3-5 min) EW also used (Grade 2C recommendation)
- Beta blockers are NOT recommended for cocaine-associated MI or ischemia prior to elimination of cocaine on theoretical considerations of coronary artery vasoconstriction and systemic hypertension from unopposed alpha adrenergic stimulation. However, this is not universally accepted and some still give beta blockers. If beta blockers are to be used, mixed alpha/beta blockers such as labetalol and carvedilol are favored over nonselective beta blockers
- Reperfusion is an important early part of management

Discharge planning and outpatient management:

Standardizing the discharge process for post-AMI patients as much as possible is crucial to improve their comfort level upon discharge and to reduce readmission rates. The section's purpose is to review necessary diagnostic tests and adjunct medicines that should be considered for any patient being discharged from MGH with AMI during their hospitalization. The most salient references for this information are: ACC/AHA guidelines for management of STEMI, as well as the ACC/AHA/SCAI Focused update on primary PCI for patients with STEMI.

A. Pre-discharge consults

Once an ACS patient is admitted to the SDU or CCU, they should be admitted using the E10/E11 admission template, which will standardize their admission orders. Included in that template are consults for:

- PT, Nutrition, smoking cessation (~50% reduction in subsequent cardiac mortality; Arch Intern Med 2000; 160: 939-44)
- Cardiac rehab (it is cost effective and associated with improvement in clinical outcomes; 20-26% lower mortality rates in modern era of secondary prevention; Am J Med. 2004; 116:682–92)
- Vaccines: Influenza & Pneumococcal vaccination
    - All patients with CVD, regardless of age, should receive PSV23. (For pts previously vaccinated, a minimum 5-year interval is recommended)
- ***Please make sure that these are ordered prior to the day of discharge.***

B. Assessment of LV function

- Class I recommendation: All patients should have a TTE performed pre-discharge in order to evaluate LV function if they did not have a ventriculogram performed during catheterization.
- In patients with significant LV systolic dysfunction, a post-discharge plan for re-evaluation ≥ 40 days later should be made, especially to address potential need for ICD therapy after allowing for recovery from myocardial stunning.

C. Lipid Lowering For Secondary Prevention

- In patients that have had ACS, lipids should be aggressively managed. Start all patients on high intensity statin that were not on one already. Recheck LDL in 6-8 weeks and if not ≤ 70, then start ezetimibe. If persistently elevated after ezetimibe, consider PCSK-9. In a patient who was reliably taking a high intensity statin prior to ACS event or cannot tolerate statin therapy, consider adding ezetimibe or PCSK-9. Consider icosapent ethyl for triglycerides > 150mg/dL.

D. Management of Diabetes

- Goal: HbA1c is < 7%. Less stringent goals may be appropriate for some patients.
- SGLT-2 inhibitors: SGLT2-inhibitors empagliflozin, canagliflozin, dapagliflozin decrease cardiovascular mortality and morbidity in T2DM patients who have CAD/high CVD risk factors (CANVAS, EMPA-REG OUTCOME, subanalysis of DECLARE-TIMI 58)
    - Adverse events: CANVAS showed increased risk of amputations, which occurred more often in those with prior history of PAD or prior amputation. Similar data has not been seen in EMPA-REG OUTCOME
- GLP-1: liraglutide lowered cardiovascular mortality and all-cause mortality (LEADER)

E. Adjunctive Medications on discharge

All AMI patients should be discharged on the following medications, unless there are contraindications:

- Aspirin: 81 mg daily for lifetime
- Second anti-platelet agent (clopidogrel, ticagrelor, prasugrel): *Submit the prescription to the patient's pharmacy as soon as this decision is made as many patients require prior authorization for these medications (ticagrelor and prasugrel) and this can hold up their discharge. Follow up to make sure affordable. Contact Interventional Cardiologist prior to changing medication*
- High intensity statin
- Beta-blocker if tolerable, can titrate as outpatient
- PPI/H2 blocker: if sending home on triple therapy, hx of GIB, or high risk as shown to decrease rate of GIB in pts on DAPT w/o increasing the rate of ischemic events (NB: observational studies that have raised concern of interaction between clopidogrel and PPI). (COGENT)
- ACE-I/ARB if anterior MI, DM, or LVEF < 40%
- PRN sublingual nitro: Most likely to be forgotten on discharge.
    - Below is an example of the instructions to give to patients regarding how to take nitroglycerin:
    - Sit or lie down if you can.
    - Place one tablet under your tongue and wait 5 minutes.
    - If you still feel chest pain, take a second tablet, and wait 5 more minutes.

  - If you still feel chest pain, take a third tablet and wait 5 more minutes.
  - If you rarely require nitroglycerin or if you feel chest pain 5 minutes after taking the third pill, call 911.
  - Always tell your doctor if you had to take this medicine
  - Keep medicine in the original bottle in a dark, dry place and check the expiration date often.
  - If you need to open the bottle, write the date you opened it in permanent marker.
  - The bottle is good for only **6 months** after it is opened.
- NSAIDs: Patients who routinely took nonsteroidal anti-inflammatory drugs (except for aspirin) before NSTEMI should ***discontinue*** these agents because of increased risks of mortality, reinfarction, hypertension, heart failure, and myocardial rupture (*Class III Recommendation: Harm*)

F. Follow up

- Appointments: The patient should be scheduled to see a cardiologist or their PCP within one month of discharge. For patients who do not have a primary cardiologist, they should be referred to the MGH MI clinic or will be set up with the PDW fellow on service. They should also be given a phone number to call for their cardiologist (even if an appointment is not scheduled at the time of discharge) so that they can call if they have symptoms.

HEART FAILURE

DEFINITIONS

Cardiomyopathy (CM): disease of myocardium. This *can* lead to heart failure, but is *not* synonymous with heart failure

- Dilated CM: dilation or impaired contraction of one/both ventricles
  - **Left ventricular internal diameter end diastole (**LVIDd) >59mm males, >53mm females
- Restrictive CM: nondilated or small ventricle(s) with diastolic dysfunction
- Hypertrophic CM: increased LV mass, with nondilated, hypertrophied LV (IVS >15mm)
- Also: arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D); unclassified CMs

Heart failure (HF): clinical syndrome characterized by typical symptoms and signs that are caused by cardiac dysfunction. Hemodynamically, it is a failure to provide commensurate cardiac output to the body, or in which output is at cost of elevated cardiac filling pressures

- Heart failure with preserved ejection fraction (HFpEF) (EF≥ 50%) accounts for 40-50% of patients with HF
- Heart failure with reduced EF (HFrEF) (EF≤ 40%) accounts for 40-50% of patients with HF
- Heart failure with midrange EF (HFmrEF) (EF 41-49%) accounts for approximately 10-20% of patients with HF

KEY PHYSIOLOGY CONCEPTS

Preload: describes the myocardial wall stretch at the end of diastole

- Most accurate measure: LV end diastolic volume (LVEDV); rarely directly measured, can be approximated by some imaging methods or bedside hemodynamic assessments
  - Closest proxy LV end-diastolic pressure (LVEDP) – can only be measured during LHC
- Closest estimate of LVEDP = left atrial pressure (LAP), when there is equal pressure gradient from ventricle to atrium
  - LAP best estimate: pulmonary capillary wedge pressure (PCWP), measured by RHC
- **AKA, in a normal heart**: LVEDV → LVEDP ≈ LAP ≈ PCWP
- In hearts with diastolic disease, ventricular volume and pressure may become uncoupled.
  - Increased LV stiffness (pericardial restriction or myo/endocardial), higher LVEDPs required to create same EDV

Afterload: describes the force opposing LV ejection

- Most accurately described as aortic impendence or elastance
- Afterload ≈ myocardial wall stress, which is defined according to Laplace's Law
  - $wall\ stress = \frac{(pressure \times radius)}{(2 \times wall\ thickness)}$.
- Increased afterload ↑ intraventricular pressure needed open the aortic valve ↑ increased wall stress.
  - If exposed to chronically ↑ afterload myocardial hypertrophy (increased thickness) to restore normal wall stress

Contractility/Inotropy: inherent capacity of the myocardium to contract independent of changes in preload or afterload.

- ↑ contractile function a/w enhanced ventricular relaxation (lusitropy),
- Frank-Starling curve relates ventricular EDV (preload) to contractility
  - ↑ in force of contraction as EDV ↑ with increasing sarcomere length and optimization of the overlap between actin + myosin filaments
  - There is a limit to this optimization after which LVEDV / EDP will increase without additional increase in SV

HISTORY & INITIAL ASSESSMENT

- HPI:
  - See table below for key symptoms
  - Identify precipitant *(medication issues, dietary indiscretion [salt, fluid, alcohol], arrhythmia, ischemia, infection)*
  - Ask for dry weight, recent weights, and functional status (number of blocks/flights of stairs they can walk)
- Medical history:
  - HF etiology, most recent EF, frequency of exacerbations
  - Other cardiac history (ischemic, valvular, arrhythmia, etc)
  - Prior testing: Prior echo, stress test, coronary CT, or CT chest that shows atherosclerosis
  - Associated conditions: HTN, DM, OSA/OHS, obesity, anemia, nutritional deficiencies
- Medications:
  - GDMT dosing
  - Diuretic dosing, any recent changes or pauses
- Social history:
  - EtOH, cocaine, methamphetamine, tobacco use
- Vitals/Exam:
  - O2 requirement compared to baseline and pulse pressure
  - See below table for common exam findings
- Studies/Imaging:
  - Labs:
    - BNP (compare to baseline), Troponin (eval for ischemia)
    - Cr (cardiorenal or low output), lactate (low output), LFTs (congestive hepatopathy)
    - Consider infectious workup if concern for causing exacerbation
    - New HF etiology labs as below
  - ECG: baseline and current EKG for signs of ischemia, arrythmia, or device malfunction that explain HF etiology and/or exacerbation
  - CXR:
    - 1) Left sided HF: pulmonary edema, pleural effusions, +- worsened cardiomegaly if large pericardial effusion
    - 2) Right sided HF: opacified upper portion of abdomen may suggest ascites
    - 3) R/o other causes of dyspnea (pneumothorax, pneumonia, ILD, etc)
  - TTE:
    - Required for every potential new diagnosis of HF

Symptoms		Signs	
Shortness of breath	Sensitivity: 84-100% Specificity: 17-34%	S3 gallop	Sensitivity: 13% Specificity: 99%
Orthopnea	Sensitivity: 22-50% Specificity: 74-77%	Tachycardia	Sensitivity: 7% Specificity: 99%
Paroxysmal nocturnal dyspnea	Sensitivity: 39-41% Specificity: 80-84%	Pedal edema	Sensitivity: 10% Specificity: 93%
Edema, abdominal distention, RUQ pain (right sided HF)	Sensitivity: 23% Specificity: 80%	Elevated JVP > 6cm	Sensitivity: 39% Specificity: 93%
		Crackles	Sensitivity: 60% Specificity: 78%
		Hepatojugular reflex	Sensitivity: 24% Specificity: 96%

		Ascites	Sensitivity: 1% Specificity: 97%

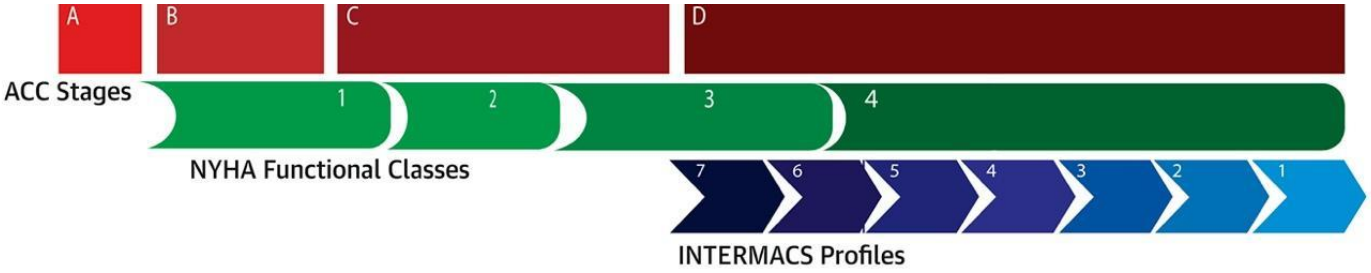
- **Not required for every patient with known HF. Useful in evaluating progressive valvular , ischemic, or pericardial disease**
- Most accurate assessment (especially of RV/LV function and valvular pathologies) is at **euvolemia,** in **sinus rhythm** and at **normal rates**

CLASSIFICATION

General classification: ACC/AHA, Stages A-D. Grades based on structural changes and symptoms

Functional classification: NYHA, Functional Classes 1-4. Grades severity of symptoms and exercise tolerance
- Since this captures symptomatic only, lowest NYHA grade starts at equivalent point to ACC/AHA B (see graphic)

Severe/decompensating: INTERMACS, Profiles 1-7. Gradations scale from NYHA III (7) to critical cardiogenic shock (1).
- Most commonly applied to advanced HF patients admitted to CCU/CS-ICU, not used in terminology as much day-to-day as other classifications above



ACC Stages

A: Patient is at high risk for developing heart failure but has no functional or structural heart disorder

B: Structural heart disorder without symptoms

C: Past or current symptoms or heart failure associated with structural disorder

D: Advanced heart disease requiring hospital-based support, transplant, or palliative care

NYHA Functional Classes

I: No limitation in normal physical activity

II: Mild symptoms with normal activity

III: Markedly symptomatic during daily activities, asymptomatic only at rest

IV: Severe limitations, symptoms even at rest

INTERMACS Profiles

Profile 1: Critical Cardiogenic Shock

Profile 2: Progressive Decline

Profile 3: Stable, But Inotrope Dependent

Profile 4: Resting Symptoms

Profile 5: Exertion Intolerant

Profile 6: Exertion Limited

Profile 7: Advanced NYHA Class III

ETIOLOGY

In general, when describing patients with the clinical syndrome of heart failure, try to delineate the type of heart failure from the underlying condition that led or put them at risk of that syndrome, if identifiable. **Example:** *62 year old male with HFrEF (EF 32%) and ischemic cardiomyopathy*

You can have heart failure syndrome without a cardiomyopathy, as cardiomyopathy refers only to the disease of the heart muscle.

Initial workup for new diagnosis of heart failure:
- **Ischemic**: EKG, troponins, HbA1c, lipids, stress test (exercise vs pharmacologic), imaging (coronary CTA), coronary angiography

- **Non ischemic – see table below. Most important studies bolded**

Type	Etiologies	Workup
Dilated *Bolded: etiologies that may or commonly present acutely*	**Infectious** ● **Viral**: flu, HIV, adeno, coxsackie, hepatitis B/C, parvovirus, CMV, EBV ● **Bacterial**: Strep (Rheumatic fever), typhoid, diptheria, brucellosis, mycobacteria, psittacosis ● **Parasitic**: toxo, T. cruzii (Chagas'), schistomiasis, trichinosis ● **Fungal**: histoplasma, crypto ● **Other**: rickettsia, syphilis, leptospira, ?Lyme	● **Viral: RVP, serologies** ● Bacterial: BCx, GAS screen (more likely historical), ● Parasitic: Toxo, T. cruzii serologies ● Fungal: serum galactomannan, 1,3B-d-glucan ● Syphilis Ab screen, Leptospira Ab, Lyme screen with reflex ● *Biopsy for path + culture may be necessary*
	Medications: ● Chemo (doxorubicin; cyclophosphamide; Herceptin) ● ART (zidovudine, didanosine, zalcitabine) ● HCQ/chloroquine ● Psychiatric/CNS meds (phenothiazines, clozapine) ● **Immune checkpoint inhibitors**	● Springboard report in Epic gives lifetime dose doxorubicin ● Serial TTEs used to monitor Herceptin ● Others gathered from patient HPI ● ICI myocarditis +- presents with dilated LV
	Rheumatologic ● SLE ● Dermatomyositis, scleroderma*, RA ● Sarcoid ● GCA, Kawasaki's disease ● **Giant cell myocarditis** ● **Eosinophilic myocarditis** ● **Hypersensitivity myocarditis**	Auto-Antibodies: ● SLE: ANA, anti-dsDNA, -Ro, -La ● Dermato: anti-Jo1, -Mi2, -MDA5 ● Scl: anti-centromere, -Scl70, RNApol III ● RA: anti-RF, -CCP ● GCA/Kawasaki: ANCA Labs: ● Sarcoid: ACEI level Path: ● GC myocarditis, eos: endomyocardial biopsy ○ *Often associated with significant arrhythmias* Imaging: ● **CXR, TTE** ● Vasculitides: CT cardiac vs CTA chest, +/- head+neck
	Genetic ● Familial or sporadic	● Genetic profiling: can be targeted to first degree

	● Duchenne's MD*, Erb dystrophy, myotonic dystrophy, FXA, ARVC	relatives, or broader screen in new diagnosis
	Endocrine ● DM ● Pheochromocytoma* ● Cushing's ● TSH (hyper or hypo*) ● GH (high* or low)	● **HgbA1c** ● Serum, urine metanephrines ● Cushing's: AM cortisol to screen; ACTH level; dex suppression to confirm ● **TSH with reflex** ● GH: IGF-1
	Toxins ● **EtOH, cocaine, amphetamines** ● Heavy metals – lead, cobalt, mercury ● Lithium ● CO	● **UTox, serum tox** ● Heavy metals screen ● Li level ● Methemoglobin
	Miscellaneous ● Tachycardia-mediated ● **Peripartum CM** ● **Heat/hypothermia** ● OSA ● Radiation induced*	● Tachycardia is diagnosis of exclusion ● PPCM: final mo. of pregnancy 5mo. post partum ● Radiation: less common now with highly specific mapping
	Deposition diseases ● Hemochromatosis*, amyloid*	● HC: screen - ferritin; confirm - HFE gene ● Amyloid: TTR scan, **SPEP/SFLC, UPEP**
Restrictive	*All "starred" above can present with restrictive picture*	
	Storage & deposition diseases ● Gaucher's disease ● Hemochromatosis ● Amyloid	● Gaucher: low β-glucosidade ● HC: ferritin + HFE ● Amyloid: TTR scan, SPEP/SFLC, UPEP
	Endomyocardial diseases ● Loeffler's endocarditis ● Endomyocardial fibrosis	● TTE + biopsy to confirm ● Loeffler's: diffuse eosinophilic infiltration ● EMF: endemic areas – Venezuela, Brazil, W. Africa, Uganda, S. India
	Genetic/Familial ● Hypertrophic phenotypes can have restrictive features	● Family history often enough to suggest ● Targeted genetic profiles in first degree relatives
	Miscellaneous ● Radiation ● Primary neoplasma/metastatic dz ● ^GH /Pheo ● Scleroderma	
Hypertrophic	Hypertension	
	Genetic/familial	● Targeted genetic profile in first degree relatives
	Endocrine ● Hypothyroidism ● Pheochromocytoma ● Acromegaly	● Serum, urine metanephrines ● **TSH with reflex** ● GH: IGF-1
	Hereditary disorders	● Biopsy and path

	● Storage diseases: *glycogen storage diseases; Fabry's* ● Friedrich's ataxia ● Neurofibromatosis	● Fabry's: alpha-GAL level (low); females also genetic test ● NF: clinical phenotype; genetics

HFrEF (EF <40%)

Guideline Directed Medical Therapy (GDMT)

- Good data that GDMT (especially multi-drug regimens) reduces mortality/hospitalizations and improves quality of life
- Goal of initial phase/initiation: start as many different classes of therapy as blood pressure and renal function allow
- Goal is not to reach target dose early. ADHF hearts are extremely sensitive – too rapid titration may lead to shock
- See table below for target doses associated with best outcomes
- Transcatheter mitral valve repair should be considered for symptomatic patients with chronic moderate-severe to severe MR despite optimal doses of GDMT (*COAPT Trial*).
- Loop diuretics are not associated with improvements in mortality, but they do improve QoL

Therapy	Target Dose	Key Trials and notes
BETA-BLOCKERS		● CIBIS-II, COPERNICUS, COMET, MERIT-HF ● Carvedilol (non-selective BB with α-blocking capacity) has greater effect on BP than metoprolol ● Contraindicated in severe conduction disease ● Use with caution in patients with tenuous cardiac index (e.g. immediately post-MI and ADHF), asthma or bronchospastic COPD
Bisoprolol	10 mg Daily	
Carvedilol	25 mg BID (<85kg) or 50 mg BID (>85kg)	
Metoprolol	200 mg Daily	
ARNI		● PARADIGM-HF, PIONEER-HF ● Do not administer with ACEi/ARBs due risk of angioedema ● Transitioning from ACE to ARNI requires a 36 hour washout period to reduce risk of angioedema (not required for ARB) ● Contraindicated in severe hepatic impairment, caution in RAS, BP < 100 and volume depletion ● ARNI is preferred over ACE-I or ARB if no contraindications
Sacubitril/valsartan	97/103mg BID	
ACE-I		● SAVE, CONSENSUS, SOLVD, V-HeFT II, ATLAS, AIRE ● Don't use if history of angioedema, bilateral RAS, symptomatic hypotension or SBP < 90 ● Can cause dry cough, angioedema, azotemia, hyperkalemia, and transient renal insufficiency upon initiation of therapy ● Reduction in eGFR of up to 30 percent in first 6-8 weeks post initiation of therapy is tolerated
Captopril	50mg TID	
Enalapril	10-20mg BID	
Lisinopril	20-40mg Daily	
Ramipril	10mg Daily	
ARBS		● CHARM-ALTERNATIVE, VAL-HeFT, HEAAL ● Consider for patients intolerant of ACE-I due to side effects (cough or angioedema); avoid ACE-I/ARB combination due to risk of hyperkalemia, hypotension and renal dysfunction
Candesartan	32mg Daily	
Losartan	150mg Daily	
Valsartan	160mg BID	
ALDOSTERONE ANTAGONIST		● RALES, EPHESUS, EMPHASIS-HF ● Avoid in patients with K > 5; be careful with use in AKI or Cr > 2.0 ● Spironolactone can cause gynecomastia and breast pain in men; eplerenone has fewer endocrine side effects
Eplerenone	50mg Daily	
Spironolactone	25-50mg Daily	
SGLT2-INHIBITORS		● DECLARE-TIMI 58, DAPA-HF, EMPA-REG, EMPEROR-Reduced ● For HF, dapagliflozin can be used eGFR ≥30 and empagliflozin for eGFR≥20
Dapagliflozin	10mg Daily	
Empagliflozin	10mg Daily	

		• Side effects: yeast infections, hypotension, volume depletion, euglycemic DKA (if DM), UTI (including complicated UTI)

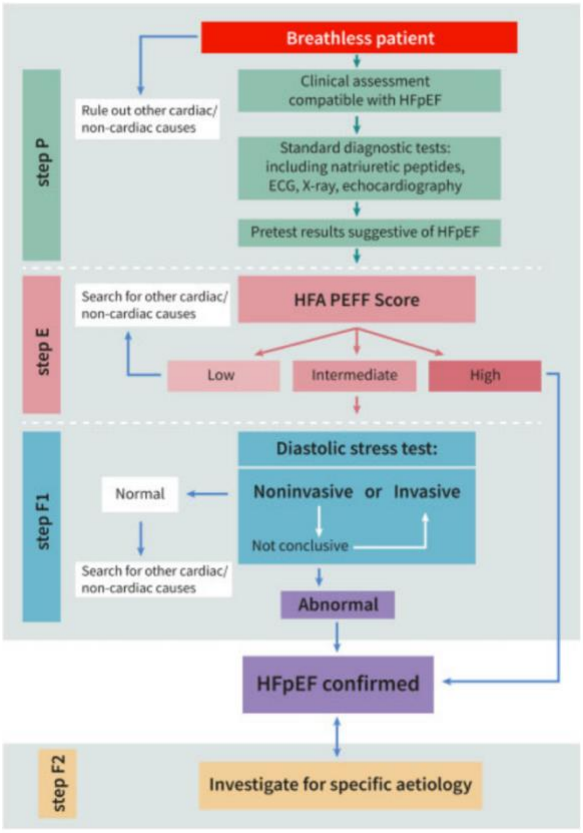
ADJUNCT THERAPIES

VASODILATORS		• V-HeFT, A-HeFT • Isosorbide mononitrate (Imdur) has not been studied and is not recommended according to ACC/AHA guidelines.
Hydralazine	75mg TID	
Isosorbide dinitrate	40mg TID	
If-CHANNEL BLOCKERS		• SHIFT, BEAUTIFUL, SHIFT-HF • Titrate to HR 50-60 BPM; indicated for patients in sinus rhythm with HR >70bpm at rest once BB therapy is maximized
Ivabradine	75 mg TID	
LOOP DIURETICS		• IV > PO for ADHF, can function as a vasodilator and decreases RA and PCWP; starting dose is typically given as 2-2.5 times home PO dose; start with intermittent bolus and consider continuous infusion if congestions is refractory to boluses • Conversions: 40 mg PO Lasix = 20 mg IV Lasix = 20 mg PO torsemide = 1 mg IV/PO Bumex
Furosemide	40-240 mg QD	
Torsemide	10-200 mg QD	
Bumetanide	1-5 mg QD	
THIAZIDE DIURETICS		• Useful in refractory diuresis. Administer 30 minutes before loop diuretic for maximum effect.
Hydrochlorothiazide	12.5-100 mg QD	
Metolazone	2.5-10 mg QD	
ICD		• SCD-HeFT, MADIT-II, DEFINITE • Primary prevention of sudden cardiac death in patients with non-ischemic dilated cardiomyopathy or ischemic heart disease at least 40 days post MI with EF of 35% or less and NYHA class II-III symptoms on GDMT with expectation of at least one year survival
CRT		• MADIT-CRT, CARE-HF, MIRACLE, RAFT • CRT is indicated for patients with LVEF 35% or less, sinus rhythm, LBBB with QRS duration of 150ms or greater and NYHA Class II-IV symptoms on GDMT; can be useful for patients with reduced EF and LBBB pattern with QRS 120-149ms or non-LBBB pattern with QRS duration of 150ms or greater • CRT should also be considered in patients on GDMT with LVEF 35% or less who are undergoing device implantation with expectation of ventricular pacing >40% of time
Iron		• FAIR-HF, CONFIRM-HF, IRONOUT-HR, RED-HF, AFFIRM-AHF • IV iron repletion (ferritin 15-100 or 100-299 with transferrin saturation < 20%) improves NYHA functional status, 6-min walk test and several quality-of-life assessments. These improvements not seen with PO iron

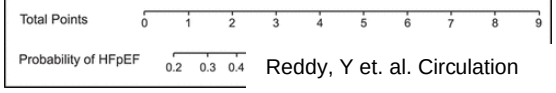
HFpEF

Diagnosis may be challenging given normal EF and non-specific signs and symptoms.

- The H_2FPEF score was developed to help distinguish HFpEF from other causes of dyspnea.
- European Society of Cardiology (ESC) has developed the HFA-PEFF diagnostic algorithm to diagnose HFpEF.
- For inpatients, RHC (+/- provocative maneuvers such as exercise) should be considered



	Clinical Variable	Values	Points
H_2	Heavy	Body mass index > 30 kg/m²	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial Fibrillation	Paroxysmal or Persistent	3
P	Pulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	Elder	Age > 60 years	1
F	Filling Pressure	Doppler Echocardiographic E/e' > 9	1
	H_2FPEF score		Sum (0-9)



Reddy, Y et. al. Circulation

	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg)	LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 #	NT-proBNP > 220 pg/ml or BNP > 80 pg/ml	NT-proBNP > 660 pg/ml or BNP > 240 pg/ml
Minor	Average E/e' 9 -14 or GLS < 16 %	LAVI 29-34 ml/m² or LVMI > 115/95 g/m² (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm	NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml	NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml
Major Criteria: 2 points	≥ 5 points: HFpEF			
Minor Criteria: 1 point	2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements			

Pieske, B. et. al. EHJ

HFpEF Treatment

- HFpEF patients often elderly and/or highly symptomatic, ∴ aim of therapy alleviate symptoms and improve QoL
  - SGLT2i (EMPEROR-PRESERVED trial). Improved outcomes for patients w/ and w/o diabetes
  - +/- spironolactone (controversial TOPCAT trial)

  Diuretics, blood pressure control, address underlying valvulopathy/arrhythmia/ischemia

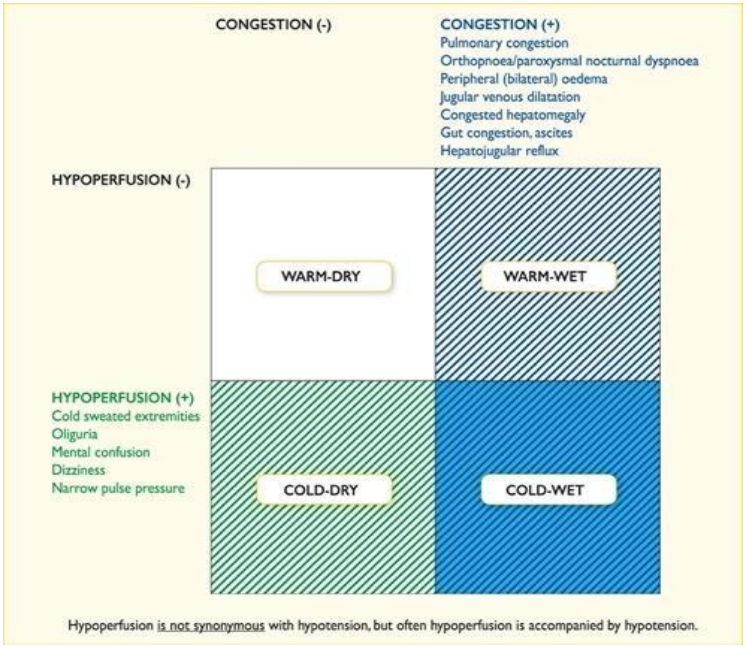
Therapy	Key Trials and Notes
SGLT2i	**EMPEROR-PRESERVED:** NEJM 2021; 385:1451-1461. Decreased cardiovascular-related death and hospitalizations regardless of concomitant diabetes
ACE-I	**PEP-CHF**: Eur Heart J 2006; 27: 2338-45. Non-significant trend toward reduced mortality.
ARB	**CHARM-Preserved**: Lancet 2003; 362: 777-8. Trend toward reduced hospitalizations **I-PRESERVE**: NEJM 2008; 359: 2456-67. No improvement of outcomes
ARNI	**PARAMOUNT**: Lancet 2012; 380: 1387-95 (vs. Valsartan). Reduced NT-proBNP ***PARAGON-HF****: NEJM 2019; 381:1609-1620. Narrowly missed primary end point (composite of HF hospitalizations or CV death) but did reduce risk in HFpEF patients at lower end of range (45-57%).* **PARALLAX**: clinicaltrials.gov (on-going trial)
Aldosterone antagonists	**TOPCAT:** NEJM 2014; 37:1383-92. Spironolactone decreased hospitalizations due to HF but no effect on mortality. **ALDO-DHF**: JAMA 2013; 309: 781-791. No effect on exercise capacity or QoL
Sildenafil	**RELAX**: JAMA 2013; 309: 1268-77. No benefit.

Imdur	**NEAT-HFpEF**: NEJM 2015;373:2314-24. Worse outcomes (reduced daily activity).
Digoxin	**DIG**: NEJM 1997;336:525-33. No effect.
Diltiazem	**MDPIT** subgroup analysis: Circ 1991; 83: 52-60

ACUTE DECOMPENSATED HEART FAILURE (ADHF)

Characterized by signs and symptoms of venous congestion ('volume overload'). This may cause hypoperfusion, i.e. shock.

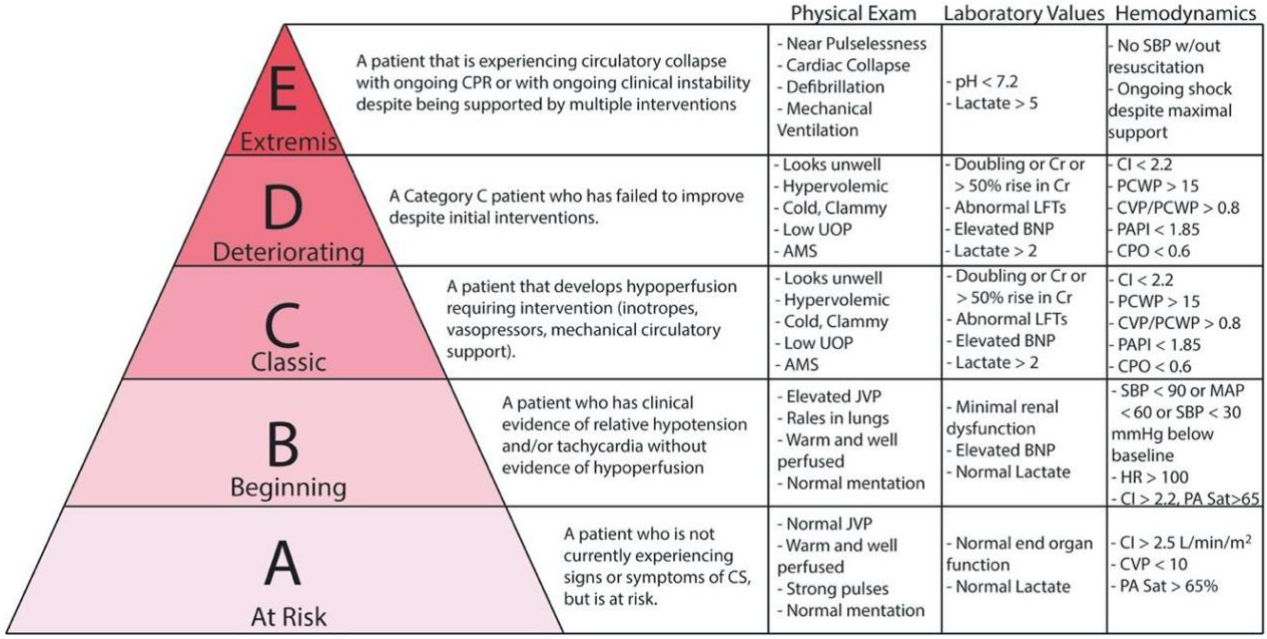
- Classify by perfusion and congestion (see table)
    - 'Wet' – proxy for elevated intracardiac pressures
    - 'Warm/Cold' – proxy for systemic vascular resistance



Specific etiologies of new, severe LV or biventricular dysfunction that are commonly seen in the CCU include:

- ACS
- Acute valvular disease
- Stress cardiomyopathy: new transient decrement in LV function (<21 days) related to emotional or physical stress
    - Takotsubo's CM: subtype characterized by i) midsegment RWMAs and basal hyperkinesis, ii) absence of CAD/ruptured plaque, iii) ischemic ECG changes and iv) exclusion of myocarditis
- Myocarditis:
    - infectious (viral, bacterial – specific etiologies above)
    - toxin/medication (immune checkpoint inhibitors most often seen)
    - inflammatory/rheumatologic (giant cell myocarditis, eosinophilic myocarditis)

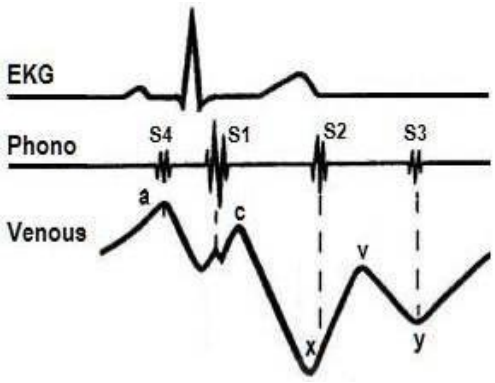
Cardiogenic shock (CS) is shock [tissue hypoperfusion] secondary to reduced cardiac output of a primary cardiac etiology. The SCAI stages of CS (A-E) can aid in the timely diagnosis and management.



- Tailored therapy: refers to use a **pulmonary artery catheter (PAC)** to obtain intracardiac pressures and hemodynamic measurements to guide therapy.
  - PAC (or Swan-Ganz): quad lumen catheter; RIJ, occasionally L RA RV **R or L main PA**
  - *Uses:* Determine etiology of shock, tailored treatment
  - *Complications:*
    - Infection/PTX/bleeding, arrhythmia, **PA rupture, IJ injury/erosion (long term)**; pulm. infarct; PE
  - *Relative CI/indications for cath lab placement:*
    - LBBB: at risk for developing RBBB and then complete heart block
    - ICD or PPM placed within the last 6 months; temp. wire
    - Valves: prosthetic/stenotic, or severe tricuspid regurgitation (challenging); TV or pulmonic valve IE
    - Severe pHTN: systolic PA pressures > 70 mmHg: ↑ risk PA rupture
    - R. heart mass (thrombus, tumor)
  - *Placement*: assess with waveform & CXR – tip at edge of middle 1/3 of thorax, ideally inferior to level of LA on CXR (West Zone 3 in V/Q map of lung

Hemodynamic Parameter	Normal Value	How to Calculate or Assess Using PAC
Cardiac output Cardiac index (CO/BSA)	CO: 4-7 L/min CI: 2.6-4.2 L/min/m^2	Thermodilution method using PAC (not accurate in shunt or TR) Fick method: $\frac{VO2}{(CaO2-CvO2)} \approx \frac{VO2}{(13.4\times Hg\times[SaO2-SvO2])}$ VO2 is measured with metabolic cart or estimated using body weight
PCWP (≈ LAP)	6-12 mmHg	PAC balloon is inflated; PCWP is measured prior to *c* wave, or if difficult to identify can average peak/trough of *a* wave. If AF (thus no *a* wave), PCWP is measured 130-160ms after QRS complex before *v*-wave; should be measured at end-expiration when intrathoracic pressure ≈ 0. See below for description of PCWP waveform.
SVR	770-1200 dynes	$\frac{(MAP-CVP}{CO}) \times 80$
PVR	< 2 Woods units / 20-130 dynes (WU x 80)	$\frac{(mPAP-PCWP}{CO}) \times 80$
CVP (≈RAP)	0-6 mmHg	CVP waveform is similar to PCWP and should be assessed similarly
MVO2 (or SvO2)	65-70%	Oxygen saturation of mixed venous blood obtained from the **pulmonary artery**
CVO2 (or ScvO2)	>65%	Oxygen saturation of central venous blood obtained from the **superior vena cava** (does not reflect venous return from lower body or myocardium)
PAPi	>2	$\frac{(PASP-PADP)}{RAP}$ Pulmonary artery pulsatility index (PAPi) is an indicator of right heart function
CPO	>0.6 W	$\frac{(MAP\times CO)}{451}$ Low cardiac power output (CPO) is a strong predictor of mortality for patients with CS

CVP/PCWP waveform
a-wave: atrial contraction, lost in AF/flutter, increased in tricuspid/mitral stenosis, cannon a-waves in junctional, VT and CHB due to contraction against closed TV/MV
c-wave: closure of TV/MV
v-wave: rapid filling of atria, TR/MR causes fusion of c and v waves into one wave (called cv-wave) and blunted x descent
x-descent: atrial relaxation
y-descent: early ventricular filling



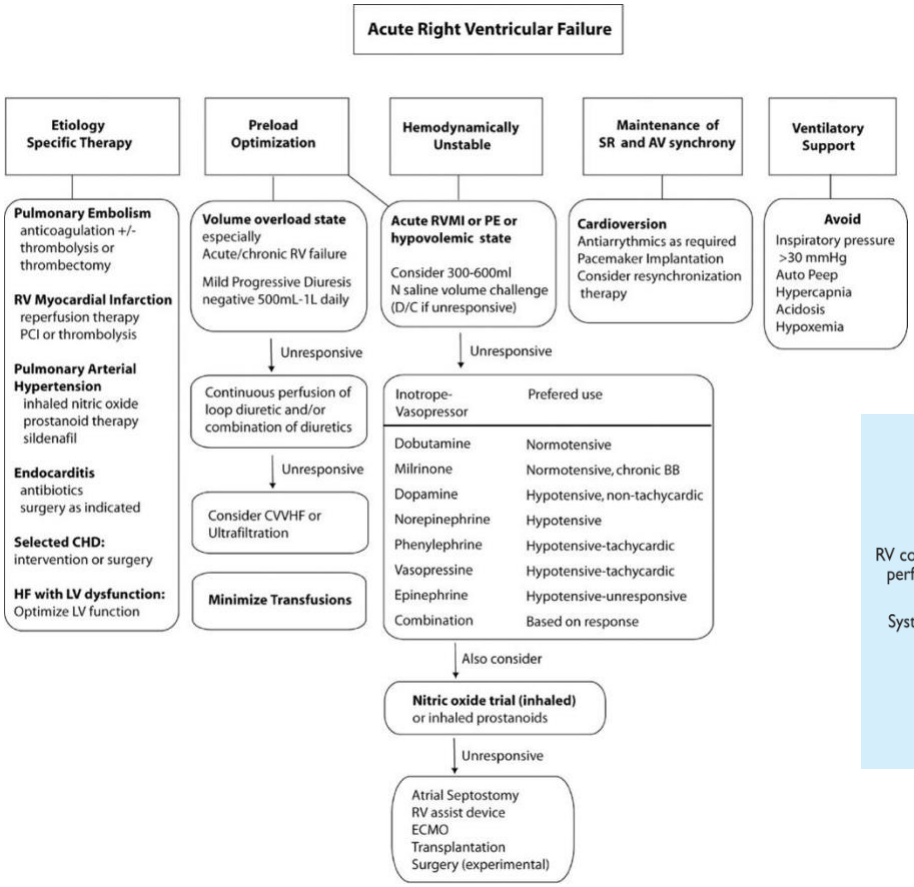
ACUTE DECOMPENSATED HEART FAILURE MANAGEMENT		
Therapy	**Target**	**Management**
Oxygen	Spo_2 >92%; 88-92% in COPD	Administer O_2 if SpO2 < 92% and sit upright. NIPPV if pulmonary edema □ PEEP helps improve oxygenation in congested alveoli. *Caution with RV failure, severe COPD, or altered mental status (inability to protect airway).* If severe hypoxemia, hypercarbia, shock or AMS □ intubation
Diuretics	PCWP < 18 CVP 8 – 12	↓CVP and PCWP to optimize Starling curve mechanics & relieve symptoms. Initial dose: IV bolus loop diuretics 2-2.5 times the home PO dose. If UOP does not augment within two hours, consider escalation in diuretic dose, Lasix □ Bumex, bolus □ gtt, or addition of a thiazide Infusion with gtt may be preferable to IV pushes in patients when hypotension is a concern for ease of titration
Vasodilators	SVR <800 SBP > 90 MAP > 65	Relieve symptoms by ↓ preload and PCWP, ↓ afterload and ↑ stroke volume NB NB if severe HTN, acute MR, acute AR
Nitroglycerin		Vasodilator effect on **veins > arteries.** Reduces cardiac O2 demand by ↓ preload; may ↓ afterload mildly as well. Gtt: initial dose 5 to 10 mcg/min up to 200 SE: headache and hypotension. Tachyphylaxis common in time.
Isosorbide dinitrate		PO version nitroglycerin. Often used in combo w/hydralazine Initial dose: 20 to 30 mg PO TID or QID SE: hypotension
Nitroprusside		↑ CO by ↓ afterload Continuous IV infusion: Initial dose 5 to 10 mcg/min SE: coronary steal (do not use in patients with un-revascularized CAD), cyanide toxicity, hypotension, increased ICP
Inotropes	CI >2.2 MvO2 >65	Consider in cold/wet patients with minimal UOP despite escalating diuretics
Dobutamine		β1>β2 agonist (inodilator) Continuous IV infusion: Initial dose 0.5 to 5mcg/kg/min SE: arrhythmias, hypotension, tachycardia and ventricular ectopy
Milrinone		PDE-3 inhibitor (inodilator) Continuous IV infusion: Initial dose 0.125mcg/kg/min Longer half-life, greater pulmonary vasodilatation, slightly less chronotropy, fewer arrhythmic events than dobutamine; caution with AKI SE: arrhythmias and hypotension
Dopamine		Adrenergic and dopaminergic receptors (inopressor) ○ Low dose: dopaminergic ○ High dose: dopaminergic and β1

		○ Large dose: alpha adrenergic Consider use if severe hypotension, unable to tolerate inodilators Continuous IV infusion: Initial dose 2 to 20mcg/kg/min SE: Arrhythmias, tachycardia, end-organ hypoperfusion
Vasopressors	CI >2.2 MvO2 >65	Use if severe hypotension and unable to tolerate inodilators SE: tachycardia, arrhythmias, end-organ hypoperfusion
Norepinephrine		α > β1 □ ↑ vasoconstriction primarily + contractility, HR Continuous IV infusion: Initial dose 0.05-1mcg/kg/min Can be useful in mixed shock
Epinephrine		α, β1, β2 leading to ↑ cardiac stimulation, ↑inotropy and ↑chronotropy ↑ Myocardial O2 consumption Continuous IV infusion: Initial dose 0.01- 0.5mcg/kg/min
Vasopressin		Risk of cardiac, digital, splanchnic ischemia; used in mixed cardiogenic & distributive
Phenylephrine		Pure α-agonist □ vasoconstriction □ ↑ afterload **Use in cardiogenic shock** with HCM physiology (increased afterload reduces LVOT gradients, reflex bradycardia beneficial) and aortic stenosis (fixed CO, want to prioritize perfusion pressure; reflex bradycardia promotes diastolic filling and maximizes output)

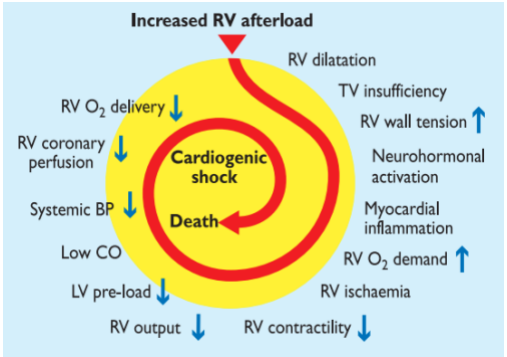
ACUTE RIGHT VENTRICULAR FAILURE (RV FAILURE)

Acute right ventricular failure: characterized by elevated right heart filling pressures in the setting of acute pulmonary hypertension (acutely elevated RV afterload).

- The RV is an embryologically, histologically and functionally different structure to the LV. It is more fibrous, with significantly less muscle mass and capability to functionally compensate for changes in pressures or volumes.
    - In the setting of acutely elevated afterload (PA pressure), the RV compensates initially by ***dilating*** – additional pressure is dissipated by creating greater volume
        - Unlike the LV, additional pressure does not increase RV stroke volume as effectively
        - As pressure/volume increases, this leads to ***increased RV wall tension*** and ***flattening of the interventricular septum (IVS)***
    - The coronary arteries fill during times of low wall tension; as RV WT ⇨, ***myocardial perfusion decreases*** ⇨ contractility ⇨ ***RV output***
    - The same pressure changes that lead to RV WT ⇨ lead to progressive flattening ⇨ ***bowing of IVS*** towards and into LV
        - This **reduces LV EDV** ⇨ reduced **preload** ⇨ ***reduced overall cardiac output***
        - **Reduced RV output also not providing as adequate preload**
    - State of **low cardiac output** ⇨ systemic HoTN ⇨ acidosis, inflammation ⇨ ⇨ pHTN, ⇨ coronary O2 delivery
    - ***This type of cardiogenic shock and spiraling deterioration is known as the RV death spiral***



Haddad, F. et. al. Circulation 2008

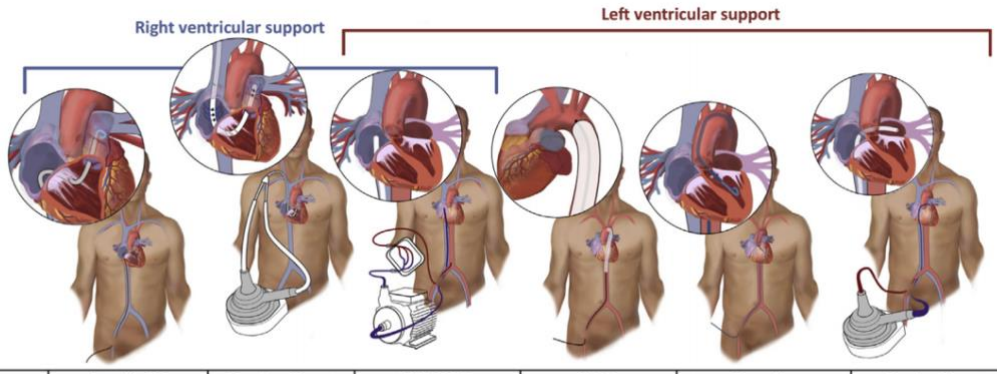


Konstantinides, S. et. al. EHJ 2014

ADVANCED THERAPIES FOR CARDIOGENIC SHOCK: MECHANICAL CIRCULATORY SUPPORT (MCS)

Indications	Contraindications
Refractory cardiogenic shock (CPO < 0.6W, CI < 2.2L/min/m^2 or elevated lactate despite pharmacologic therapy)	Anoxic Brain Injury
	Irreversible End Organ Failure
	Prohibitive Vascular Access
High risk interventional procedures	DNR

- Type of MCS device is determined by indication, INTERMACS profile, predominant ventricle involved (left, right or both) and presence of hypoxemia
- **If concern for worsening cardiogenic shock on pharmacotherapy, the CARDIOGENIC SHOCK team (staffed by HCICU Attending) should be paged at 29151 for early consideration of MCS**.
- *As IABP is the main therapy residents are exposed to, this will be discussed in detail next. Please see chart below for brief description and comparison of other available MCS options.*



	Impella RP	TandemHeart RA-PA	VA-ECMO	IABP	Impella (2.5, CP, 5.0, 5.5)	TandemHeart LA-FA
Flow	max 4.0 l/min	max 4.0 l/min	max 7.0 l/min	0.5 l/min	2.5 - 5.5 l/min	max 4.0 l/min
Pump Speed	33000 rpm	max 7500 rpm	max 5000 rpm	NA	max 51,000 rpm	max 7500 rpm
Mechanism	Axial flow continuous pump (RA-to-PA)	Centrifugal flow continuous pump (RA-to-PA)	Centrifugal flow continuous pump (RA-to-AO)	Balloon inflation-deflation (AO)	Axial flow continuous pump (LV-to-AO)	Centrifugal flow continuous pump (LA-to-AO)
Cannula Size	22 F venous	29 F venous	14-19 F arterial 17-21 F venous	7-8 F arterial	13-21 F arterial	12-19 F arterial 21 F venous
Insertion/Placement	Femoral vein	Internal jugular vein	Femoral vein Femoral artery	Femoral artery Axillary artery	Femoral artery Axillary artery	Femoral artery Femoral vein
LV Unloading	-	-	-	+	+to+++	++
RV Unloading	+	+	++	-	-	-
Cardiac Power	-	-	↑↑	↑	↑↑	↑↑
Afterload	-	-	↑↑	↓	↓↓	↑
Coronary Perfusion	-	-	-	↑	↑	-
Considerations	• *RECOVER RIGHT: 73% survival-to-30 days in RVF post LVAD, AMI or cardiotomy* • *May 2019 - FDA post-approval study: 33% survival-to-30 days*	• *IJ access may facilitate early ambulation*	• *Bi-V + oxygenation support for CS following:* *- AMI, ADHF or cardiac arrest* *- Cardiotomy* *- Myocarditis* *- Allograft rejection*	• *Requires stable cardiac rhythm and native heart function* • *May consider in select cases of post-AMI mechanical complications*	• *June 2008 – FDA 510(k) approval for HR-PCI* • *April 2016: Expanded Indication for CS* • *Contraindicated with mechanical aortic valve, LV thrombus*	• *Requires transseptal access* • *Oxygenator may be added to the circuit*

Tehrani, B. et. al. JACC HF. 2020

INTRA-AORTIC BALLOON PUMP (IABP)

A. Access

- 30-50 cc balloon; inserted into the descending aorta via percutaneous femoral artery access, less commonly via surgical cut-down of the axillary artery.
- Correct positioning: tip of the IABP should be 1cm distal to L subclavian so as not to occlude proximal (L subclavian, L common carotid) or distal (splenic or renal) arteries
    - *Daily CXR to assess placement:* tip radio-opaque, should be at L 2nd intercostal space, at level of L main bronchus

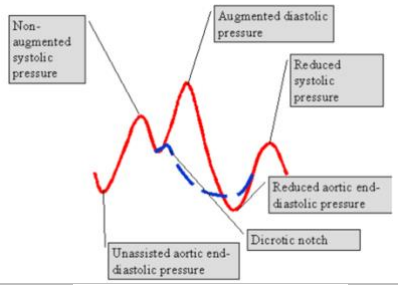
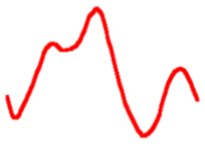
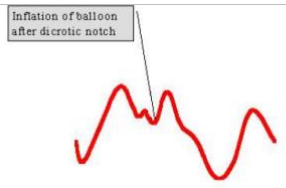
B. Indications
Cardiogenic shock and hemodynamic instability after a STEMI refractory to pharmacological management (Class IIa based on findings from *IABP-SHOCK II*)
Mechanical complications of MI (VSD, severe MR)
Refractory ischemia (intractable angina with impaired LV function or large territory infarct, refractory polymorphic VT)
Prophylactic placement prior to high risk procedures (PCI, CABG)
Inability to wean from cardiopulmonary bypass after
C. Contraindications
Severe aortic regurgitation
Severe bilateral peripheral arterial disease
Aortic dissection, aneurysm, or intramural hematoma
Severe coagulopathy or sepsis

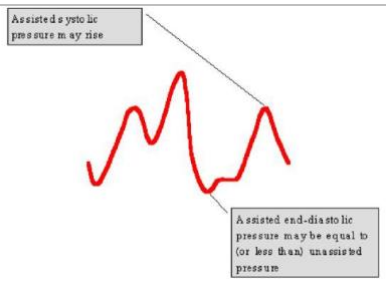
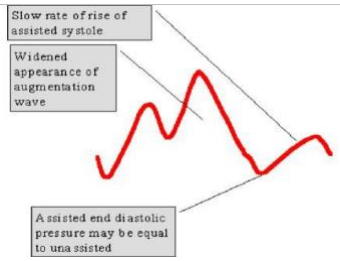
Mandawat, A. Rao, S. Circulation. 2017

D. Mechanism

- *Counter pulsation:* Inflates with helium in diastole, actively deflates during systole.
- Key principles:
    - Amount of blood displaced is proportional to the volume of the balloon
    - LV and aortic diastolic filling times are inversely proportional to heart rates; shorter diastolic filling times (higher heart rates) produce less balloon augmentation per unit time
    - as aortic compliance ↑ (or SVR decreases), the magnitude of diastolic augmentation decreases

IABP Waveform

	**Normal**: IABP inflates after AoV closes (dicrotic notch), leading to diastolic augmentation > than SBP. Balloon inflation leads to a sharp and deep V at the dicrotic notch. Deflation starts immediately before the opening of the aortic valve, leading to reduced end-diastolic pressure.
	**Early Inflation**: Loss of deep V □ premature AoV closure □ incomplete LV emptying, AI, ↑LV EDV / LV EDP, ↑ afterload and ↑ myocardial oxygen demand.
	**Late Inflation**: Deep V becomes a W □ decreased augmented coronary perfusion, ↓ O2 to coronaries and reduced overall benefit of the IABP.

	**Early Deflation**: Premature deflation increase aortic pressure prior to isovolumetric contraction ↑ afterload and ↑ myocardial demand. Diastolic augmentation is also suboptimal.
	**Late Deflation**: IABP remains inflated during isovolumetric contraction, thus the LV is contracting against an inflated balloon leading to ↑↑ increase in afterload. **This requires immediate attention.**

E. Complications:

- Anemia and thrombocytopenia
- Insertion site complications (bleed, infection, aneurysm, fistula)
- Limb ischemia (**daily pulse checks and vascular exam;** requires device removal)
- Vascular injury including dissection or pseudoaneurysm (12-40%) or stroke
- Balloon rupture (suspect if blood seen in helium line; device detect, will attempt to aspirate helium from aorta to prevent gas embolism).

Any suspected complication should prompt an <u>immediate</u> call to the fellow/attending or HCICU Intensivist.

F. **Weaning/Removal**:

- Depending on hemodynamic status and indication for device, the IABP is programmed to assist every beat (1:1) or less often (1:2, 1:4, 1:8). Improvements decrease cycling frequency
- Thrombosis risk increases at frequencies <1:1 (stasis) – AC required for these
- Wean stepwise, with assessment of hemodynamics, rhythm, symptoms during each phase. Before removal, return to 1:1 x hours due to risk of thrombus dislodgement
- Remove after holding heparin x hours, generally when PTT <40
- *Per policy at MGH, IABPs are removed only by fellows or more senior*

ADVANCED THERAPY: LONG-TERM DURABLE MECHANICAL CIRCULATORY SUPPORT (LT-MCS)

Indications	Absolute Contraindications
NYHA functional class IIIB-IV, EF < 25% and at least one of the following criteria: ● INTERMACS profile 2-4 ● Inotrope or acute MCS dependence ● Progressive end-organ dysfunction ● Peak VO_2 < 14 ml/kg/min (or 12 ml/kg/min on beta blockers) ● Acute MCS dependence ● To reverse elevated PVR or renal failure in potential heart transplant candidates ● To allow time for transplant contraindications to be reversed such as recent cancer, obesity and recovery drug/alcohol dependence	Irreversible hepatic, renal or neurological disease
	Medical non-adherence
	Active mental illness or psychosocial instability
	Relative Contraindications
	Age > 80
	Morbid obesity (BMI >35) or cachexia
	Active systemic infection or prolonged intubation
	Untreated malignancy
	Severe peripheral artery disease or cerebrovascular disease
	Significant aortic insufficiency unable to be corrected
	Drug, tobacco or alcohol use within 6 months

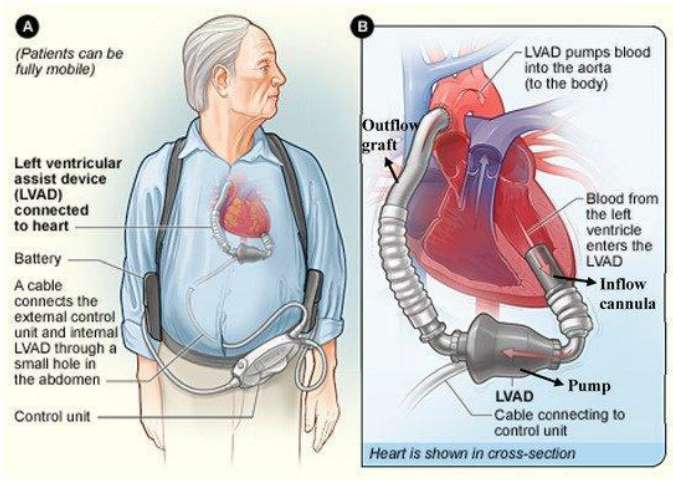
According to indication, LT-MCS use may be categorized as a:

- **Bridge to candidacy**: use of LT-MCS to improve end-organ function (or buy time) for an ineligible patient to become eligible for heart transplantation
- **Bridge to transplantation**: use of LT-MCS to keep patient alive who is otherwise at high risk of death before transplantation until a donor organ becomes available
- **Bridge to recovery**: use of LT-MCS to keep a patient alive until cardiac function recovers sufficiently to remove MCS
- **Destination therapy**: use of LT-MCS as an alternative to transplantation in patients with end-stage HF ineligible for transplantation or long-term waiting for heart transplantation

Devices: LT-MCS most commonly refer to ventricular assist devices (VAD) which are FDA approved to provide support to the left ventricle (LVAD).

- NB: VADs are also used off-label for RV support (RVAD) or to support both ventricles (BiVAD). RV support cannot be done outside of an ICU.
- Total artificial heart (TAH) is FDA approved for biventricular support but is not available at MGH.

Principles of VAD



- Blood to LV pump via inflow cannula (surgically implanted in apex) blood to ascending aorta via outflow graft
- Driveline: Surgically tunneled cable that connects the pump to an external control unit which operates and monitors pump function (LVAD speed, flow, power, pulsatility index). Driveline exits the body through abdominal wall. The external controller is connected to a power source.
- The rotor or impeller within the pump propels blood by spinning at a high speed. Blood flow is proportional to pump speed though the relationship is not linear. The speed is set by the provider to ensure adequate LV unloading. Inadequate loading may result in pulmonary edema while excessive unloading could lead to suction events, resulting in hypotension or arrythmias.
- **Continuous flow devices do not generate a pulse**. However, the interaction with native ventricular function leads to phasic changes in blood flow through the LVAD called the pulsatility index for the HeartMate II and is displayed as the waveform for HVAD.
- Given risk of thrombus with continuous flow devices, VADs mandate anticoagulation (heparin warfarin)

Complications intrinsic to the pump	
Driveline	Accidental mechanical impact/pulling cable, weight gain. Treatment of lead fractures is a repair but some may require pump exchange.
Pump Malfunction	Mainly a consequence of pump thrombosis; technical failure can occur less commonly
Outflow graft occlusion	Due to thrombus, stenosis, compression, malposition. Pump flow decreases, and power increases to maintain speed. Work-up includes a CT scan of chest.
Complications related to pump-patient interface	
Infection	Driveline infections and blood stream infections may mandate chronic antibiotic therapy, device exchange or emergent transplantation depending on the clinical severity
Pump thrombosis	Hemodynamic changes seen = power spikes (abrupt increases in power consumption), slow increase in power requirements, clinical evidence of hemolysis (abrupt rise in LDH). Early pump thrombosis pump exchange or heart transplant; late pump thrombosis sometimes treated with IV heparin
GI bleeding	Common cause of hospital readmissions both early and later. Often no intervenable source. AC interrupted until bleeding resolves; recurrent bleeding lower target INR.

CVA	Leading cause of long-term mortality; VAD patients are at risk of both ischemic and hemorrhagic stroke. Ischemic stroke = emboli from pump thrombosis. Hemorrhagic stroke = due to the need for chronic AC or risk of hemorrhagic conv. of isch. NCHCT for any acute mental status or neurologic change.
Arrythmia	Burden of arrythmias is high in LT-MCS; reasonably well tolerated with low risk of immediate hemodynamic collapse since output independent of native myocardium
Aortic insufficiency	In ~10 to 53%; fusion of commissures and degenerative changes of cusps from persistent aortic valve closure. Assessed by TTE.
RHF	**Risk of developing right heart failure is an important consideration in assessing candidacy for LVAD**; exacerbation of pre-existing RHF, or by changes to RV structure (septal bowing) due to off-loading of the left ventricle. Assessment of PVR critical.

Alarm type	Advisory (non-critical)	Critical	Evaluation and Management
Low flow or suction	• Speed too high/ low • Hypovolemia • RV dysfunction • Tamponade • HTN/Arrhythmia • Inflow/outflow obstruction	Same differential as advisory alarm, but associated with extremely low flow	Obtain MAP, ECG, TTE Trial of volume (albumin) if suction Manage HTN/treat VT **Page HF or VAD pager (11045)**
Low power	• Power disconnected • Low battery power	Driveline disconnect Depleted batteries Power modules disconnect	Examine driveline Replace batteries **Page HF or VAD pager (11045)**
High power	• Pump thrombosis • Poorly controlled HTN • Electric fault	Same as advisory column.	LDH, LFT, INR, U/A, CBC **Treat HTN. Page HF service or VAD pager**

ORTHOTOPIC HEART TRANSPLANT

Indications	Absolute Contraindications	Relative Contraindications
End-stage HF with severe symptoms, poor prognosis and no remaining alternative treatment options Peak VO2 ≤14 ml/kg/min favor listing	• Systemic illness with life expectancy < 2 years • Fixed pulmonary hypertension – i.e. pulmonary pressures do not improved with improved LV function *(theoretically could receive heart-lung)*	• Age > 72 • Active infection (except VAD related) • Severe comorbidities including DM, PAD, CVA, PUD, morbid obesity, cachexia) • Renal/liver failure – *can be dual listed* • Active mental illness or psychosocial instability • Medication non-adherence • Recent HIT • EtOH/tobacco/drug use

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Evaluation of the Heart Transplant Candidate:

- Clinical History and Physical Examination
- Laboratory Evaluation: Complete Blood Count, Basic Metabolic Panel, Liver Function Tests, Urinalysis, Coagulation Studies, Thyroid Evaluation, Urine Drug Screen, Alcohol Level, HIV Testing, Hepatitis Testing, Tuberculosis Screening, CMV IgG and IgM, RPR/VDRL, Panel Reactive Antibodies, ABO and Rh Blood Type, Lipids, Hemoglobin A1c
- Chest X-Ray, Pulmonary Function Testing
- EKG
- Right and left heart catheterization
- Cardiopulmonary exercise testing
- Age appropriate malignancy screening
- Psychosocial evaluation (including substance abuse history, mental health, and social support)
- Financial Screening

Tier	
1.	i. VA ECMO (up to 7 days) ii. Non-Dischargeable BIVAD iii. Mechanical circulatory support with life threatening ventricular arrhythmia
2.	i. Intra-aortic balloon pump (up to 14 days) ii. Acute percutaneous endovascular circulatory support (up to 14 days of support) iii. Ventricular tachycardia / Ventricular Fibrillation, mechanical circulatory support not required iv. Mechanical circulatory support with device malfunction / device failure v. Total Artificial Heart vi. Dischargeable BIVAD or RVAD
3.	i. LVAD for up to 30 days ii. Multiple Inotropes of Single High-Dose Inotrope With Continuous Hemodynamic Monitoring iii. Mechanical Circulatory Support with Device Infection iv. Mechanical Circulatory Support with Thromboembolism v. Mechanical Circulatory Support with Device Related Complications Other Than Infection, Thromboembolism, Device Malfunction/Failure, and Life Threatening Ventricular Arrhythmias
4.	i. Diagnosis of Congenital Heart Disease (CHD) with: a. Unrepaired/incompletely repaired complex CHD, usually with cyanosis b. Repaired CHD with two ventricles c. Single ventricle repaired with Fontan or modifications ii. Diagnosis of ischemic heart disease with intractable angina iii. Diagnosis of hypertrophic cardiomyopathy iv. Diagnosis of restrictive cardiomyopathy v. Stable LVAD patient after 30 days vi. Inotropes without hemodynamic monitoring vii. Diagnosis of amyloidosis viii. Retransplant
5.	i. Approved combined organ-transplants: heart-lung, heart-liver, heart-kidney
6.	i. All remaining active candidates
7.	i. Inactive / Not Transplantable

Immunosuppression: Post-transplant immunosuppression typically consists of a triple regimen that includes calcineurin inhibitors (such as cyclosporine and tacrolimus), purine synthesis inhibitors (such as MMF and azathioprine) and corticosteroids.

- MMF is superior to azathioprine in preventing rejection and mortality.
- Steroids prescribed in high doses initially with gradual taper starting at 6 months post-transplantation.
- Patients undergo routine cardiac biopsies to grade level of rejection post-transplant (per below table)

Early Complications Following Cardiac Transplantation	
Primary graft dysfunction	Most common cause of mortality in 1st month post transplant. Risk factors: older donor or recipient age, female donor, non-head trauma cause of death, CAD in donor, prolonged ischemic time. Assess: TTE. Management: inotropes; potential MCS
Acute right ventricular failure	Preoperative PH is associated with high incidence of RHF and perioperative mortality.
Conduction abnormalities	Denervation of donor heart loss of PNS efferents from vagus to SA node and loss of SNS efferents to the atria/ventricles. RBBB/LBBB may result from trauma to conduction system. Epicardial pacing used intraoperatively to maintain CO with HRs 100-120.
Late Complications Following Cardiac Transplantation	
Chronic Allograft Vasculopathy	Accelerated atherosclerosis of blood vessels after cardiac transplantation. Risk factors include older donor/recipient age, DM, HTN, mismatch of body size and HLA mismatch. Due to denervation of donor heart, patients do not have typical anginal pain but presents with HF, arrythmia or SCD. IVUS and coronary angiogram 4-6 weeks after transplant at min. Non-invasive testing with stress TTE, MRI or PET can also be done at regular intervals. Treatment: stenting with PCI if disease is localized; if diffuse, modify IS, statins
Infection	Common in acute and chronic setting post-transplant. Posttransplant, prophylaxis for PJP, HSV, toxoplasmosis and oral candidiasis is started. CMV -Recipients of CMV+ hearts: antiviral prophylaxis.
Chronic Kidney Disease	Up to 50% of patients 5 years after transplant. Risk factors: older age, female, lower eGFR pretransplant, pretransplant inotrope/MCS use, CNI use.
Steroid related complications	All patient should receive calcium/vitamin D and possibly bisphosphonates. Consider early withdrawal of steroids is possible.
Cardiac Rejection	
Hyperacute rejection	Occurs immediately after aortic cross-clamp is removed and the donor heart is exposed to recipients blood cells. This is now uncommon due to cross-matching of blood type and panel reactive antibodies.
Acute cellular rejection	Mediated by the recipient's T cells recognizing donor HLA molecules; characterized by an inflammatory infiltrate on EMB. Classified based on the severity of lymphocytic infiltrate and myocyte: ● Grade 0 (no rejection), ● Grade 1R (mild), ● Grade 2R (moderate) ● Grade 3R (severe) MGH also uses the 1990 ISHLT histologic criteria, ● Grade 0 (no evidence of ACR) ● Grade 1A (focal infiltrate without myocyte damage) ● Grade 1B (diffuse infiltrate without myocyte damage) ● Grade 2 (one focus of infiltrate with associated myocyte damage) ● Grade 3A (multifocal infiltrate with myocyte damage) ● Grade 3B (diffuse infiltrate with myocyte damage) ● Grade 4 (diffuse injury with extensive myocyte damage) Treatment includes high dose corticosteroids or antithymocyte antibodies if no response to steroids. Repeat EMB is performed 1-2 weeks after treatment for follow-up.
Antibody mediated rejection	● Donor antigens and recipient antibodies forms an antigen-antibody complex or membrane attack complex that results in endothelial and vascular injury. ● Diagnosis is confirmed by presence of donor specific antibodies and via EMB with evidence of complement activation ● Management includes IVIG, plasmapheresis, antilymphocyte antibodies and high dose steroids.

References

1. 2016 ESC Guidelines. PMID: 27207191
2. 2013 ACCF/AHA Guidelines. PMID: 23741058
3. 2017 ACC/AHA/HFSA Guidelines. PMID: 28461259
4. 2021 Update to ACC Guidelines. PMID: 33446410
5. Zipes, Douglas P. et al. *Braunwald's Heart Disease : A Textbook of Cardiovascular Medicine.* Eleventh edition. Elsevier, 2019
6. Heart Failure: Diagnosis, Management and Utilization PMID: 27367736
7. Advanced Heart Failure: Epidemiology, Diagnostics and Therapeutic Approaches PMID: 32525126
8. Wireless pulmonary artery hemodynamic monitoring in chronic heart failure: a randomized control trial PMID: 21315441
9. Transcatheter mitral valve repair in patients with heart failure PMID: 30280640
10. Right ventricular function in cardiovascular disease, Part II PMID: 18378625
11. A simple evidence based approach to help guide diagnosis of heart failure with preserved ejection fraction PMID: 29792299
12. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm PMID: 32133741
13. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. PMID: 25173341
14. CIBIS-II: "The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomized trial". The Lancet. 1999. 353(9146):9-13. PMID: 10023943
15. COPERNICUS: Packer M, et al. "Effect of Carvedilol on the Morbidity of Patients With Severe Chronic Heart Failure". Circulation. 2002. 106(17):2194-9. PMID: 12390947
16. COMET: Poole-Wilson PA, et al. "Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial". The Lancet. 2003. 362(9377):7-13. PMID: 12853193
17. MERIT-HF: Fagerberg B, et al. "Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure". The Lancet. 1999. 353(9169):2001-7. PMID: 10376614
18. PARADIGM-HF: McMurray JJV, et al. "Angiotensin-neprilysin inhibition versus enalapril in heart failure". The New England Journal of Medicine. 2014. 371(11):993-1004. PMID: 25176015
19. PIONEER-HF: Velazquez EJ, et al. "Angiotensin-Neprilysin Inhibition in Acute Decompensated Heart Failure". The New England Journal of Medicine. 2018. ePub 2018-11-11:1-10. PMID: 30415601
20. SAVE: Pfeffer MA, et al. "Effect of Captopril on Mortality and Morbidity in Patients with Left Ventricular Dysfunction after Myocardial Infarction — Results of the Survival and Ventricular Enlargement Trial". The New England Journal of Medicine. 1992. 327(10):669-677. PMID: 1386652
21. CONSENSUS Trial Study Group. "Effects of enalapril on mortality in severe congestive heart failure, results of the cooperative north Scandinavian enalapril survival study". The New England Journal of Medicine. 1987. 316(23):1429-35. PMID: 2883575
22. SOLVD: Yusuf S, et al. "Effect of Enalapril on Survival in Patients with Reduced Left Ventricular Ejection Fractions and Congestive Heart Failure". The New England Journal of Medicine. 1991. 325(5):293-302. PMID: 2057034
23. V-HeFT II: Cohn JN, et al. "A Comparison of Enalapril with Hydralazine–Isosorbide Dinitrate in the Treatment of Chronic Congestive Heart Failure". The New England Journal of Medicine. 1991. 325(5):303-310. PMID: 2057035
24. ATLAS: “Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. ATLAS Study Group” Circulation. 1999 Dec 7;100(23):2312-8. PMID: 10587334
25. AIRE: “Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. The Acute Infarction Ramipril Efficacy (AIRE) Study” The Lancet. 1993 Oct 2;342(8875):821-8. PMID: 8104270
26. CHARM-ALTERNATIVE: Granger CB, et al. "Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-Alternative trial". The Lancet. 2003. 362(9386):772-776. PMID: 13678870
27. VAL-HeFT: Cohn JN, et al. "A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure". The New England Journal of Medicine. 2001. 345(23):1667-75. PMID: 11759645
28. HEAL: Konstam MA, et al. "Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure". The Lancet. 2009. 374(9704):1840-1848. PMID: 19922995
29. RALES: Pitt B, et al. "The effect of spironolactone on morbidity and mortality in patients with severe heart failure". The New England Journal of Medicine. 1999. 341(10):709-717. PMID: 10471456
30. EPHESUS: Pitt B, et al. "Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction". The New England Journal of Medicine. 2003. 348(14):1309-21. PMID: 12668699

31. EMPHASIS-HF: Zannad F, et al. "Eplerenone in patients with systolic heart failure and mild symptoms". The New England Journal of Medicine. 2011. 364(1):11-21. PMID: 21073363
32. DECLARE-TIMI 58: Wiviott SP, et al. "Dapagliflozin and cardiovascular outcomes in type 2 diabetes". The New England Journal of Medicine. 2019. 380(4):347-357. PMID: 30415602
33. DAPA-HF: McMurray JJV, et al. "Dapagliflozin in Patients With Heart Failure and Reduced Ejection Fraction". The New England Journal of Medicine. 2019. 381(21):1995-2008. PMID: 31535829
34. EMPA-REG: Zinman B, et al. "Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes". The New England Journal of Medicine. 2015. 373(22):2117-28. PMID: 26378978
35. EMPEROR-Reduced: Packer M, et al. "Cardiovascular and renal outcomes with empagliflozin in heart failure". The New England Journal of Medicine. 2020. 383(15):1413-1424. PMID: 32865377
36. V-HeFT: Cohn JN, et al. "Effect of vasodilator therapy on mortality in chronic congestive heart failure". The New England Journal of Medicine. 1986. 314(24):1547-52. PMID: 3520315
37. A-HeFT: Taylor AL, et al. "Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure". The New England Journal of Medicine. 2004. 351(20):2049-2057. PMID: 15533851
38. SHIFT: Swedberg K et al. "Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study". The Lancet. 2010. 376(10):875-885. PMID: 20801500
39. BEAUTIFUL: “Ivabradine for patients with stable coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): a randomised, double-blind, placebo-controlled trial.” The Lancet. 2008 Sep 6;372(9641):807-16. PMID: 18757088
40. SHIFT-HF: “Influence of Cardiovascular and Noncardiovascular Co-morbidities on Outcomes and Treatment Effect of Heart Rate Reduction With Ivabradine in Stable Heart Failure (from the SHIFT Trial).” Am J Cardiology. 2015 Dec 15;116(12):1890-7. PMID: 26508709
41. DOSE: Felker GM, et al. "Diuretic strategies in patients with acute decompensated heart failure". The New England Journal of Medicine. 2011. 364(9):797-805. PMID: 21366472
42. SCD-HeFT: Bardy GH, et al. "Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure". The New England Journal of Medicine. 2005. 252(3):225-37. PMID: 15659722
43. MADIT-II: Moss AJ, et al. "Prophylactic Implantation of a Defibrillator in Patients with Myocardial Infarction and Reduced Ejection Fraction". The New England Journal of Medicine. 2002. 346(12):877-883. PMID: 11907286
44. DEFINITE: Kadish A, et al. "Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy". The New England Journal of Medicine. 2004. 350(21):2151-2158. PMID: 15152060
45. MADIT-CRT: Moss AJ, et al. "Cardiac-resynchronization therapy for the prevention of heart-failure events". The New England Journal of Medicine. 2009. 361(14):1329-1338. PMID: 19723701
46. CARE-HF: “The effect of cardiac resynchronization on morbidity and mortality in heart failure.” The New England Journal of Medicine 2005 Apr 14;352(15):1539-49. PMID: 15753115
47. MIRACLE: Abraham W T, et al. "Cardiac Resynchronization in Chronic Heart Failure". The New England Journal of Medicine. 2002. 346(24):1845-1853. PMID: 12063368
48. RAFT: Tang AS, et al. "Cardiac-resynchronization therapy for mild-to-moderate heart failure". The New England Journal of Medicine. 2010. 363(25):2385-2395. PMID: 21073365
49. PEP-CHF: “The perindopril in elderly people with chronic heart failure (PEP-CHF) study”. Eur Heart J 2006; 27: 2338-45. PMID: 16963472
50. CHARMED-PRESEVERED: Yusuf S, et al. "Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: The CHARM-Preserved Trial". The Lancet. 2003. 362(9386):777-781. PMID: 13678871
51. I-PRESERVE: “Irbesartan in patients with heart failure and preserved ejection fraction.” The New England Journal of Medicine. 2008 Dec 4;359(23):2456-67. PMID: 19001508
52. PARAMOUNT: “The angiotensin receptor neprilysin inhibitor LCZ696 in heart failure with preserved ejection fraction: a phase 2 double-blind randomised controlled trial”. The Lancet. 2012 Oct 20;380(9851):1387-95. PMID: 22932717
53. PARAGON-HF: Solomon SD, et al. "Angiotensin–neprilysin inhibition in heart failure with preserved ejection fraction". The New England Journal of Medicine. 2019. 381(17):1609-1620. PMID: 32187481
54. PARALLAX: “Angiotensin receptor neprilysin inhibition versus individualized RAAS blockade: design and rationale of the PARALLAX trial” ESC Heart Failure 2020 Jun;7(3):856-864. PMID: 32297449
55. TOPCAT: Pitt B, et al. "Spironolactone for heart failure with preserved ejection fraction". The New England Journal of Medicine. 2014. 370(15):1383-1392. PMID: 24716680
56. RELAX: Redfield MM, et al. "Effect of Phosphodiesterase-5 Inhibition on Exercise Capacity and Clinical Status in Heart Failure with Preserved Ejection Fraction". JAMA. 2013. 309(12):1268-1277. PMID: 23478662
57. NEAT-HFpEF: Redfield MM, et al. "Isosorbide mononitrate in heart failure with preserved ejection fraction". New England Journal of Medicine. 2015. 373(24):2314-2324. PMID: 26549714
58. DIG: Gorlin R, et al. "The effect of digoxin on mortality and morbidity in patients with heart failure". The New England Journal of Medicine. 1997. 336(8):525-533. PMID: 9036306

59. MDPIT: “Diltiazem increases late-onset congestive heart failure in postinfarction patients with early reduction in ejection fraction. The Adverse Experience Committee; and the Multicenter Diltiazem Postinfarction Research Group” Circulation. 1991 Jan;83(1):52-60. PMID: 1984898
60. A standardized and comprehensive approach to the management of cardiogenic shock. PMID: 33121700
61. Intra-aortic balloon support for myocardial infarction with cardiogenic shock. PMID: 22920912
62. Percutaneous Mechanical Circulatory Support Devices in Cardiogenic Shock. PMID: 28500136
63. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high risk percutaneous coronary intervention. PMID: 22935569
64. Percutaneous Mechanical Circulatory Support versus Intra-aortic balloon pump in cardiogenic shock after acute myocardial infarction. PMID: 27810347
65. Recover I: a multicenter prospective study of Impella 5.0/LD for post-cardiotomy circulatory support. PMID: 22405676
66. Impella ventricular support in clinical practice: Collaborative Viewpoint from a European expert user group PMID: 26363632
67. Left ventricular assist devices 101: shared care for general cardiologist and primary care. PMID: 31635239
68. Temporary circulatory support for cardiogenic shock. PMID: 32682486
69. A standardized and comprehensive approach to the management of cardiogenic shock. PMID: 33121700
70. 2019 EACTS Expert consensus on long-term mechanical circulatory support. PMID: 31100109
71. Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion. PMID: 25281189
72. Rihal CS et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care. *J Am Coll Cardiol.* 2015;65(19), 2140-2141. PMID: 25861962
73. Vieira JL, Ventura HO, Mehra MR. Mechanical circulatory support devices in advanced heart failure: 2020 and beyond. Prog Cardiovasc Dis. 2020 Sep-Oct;63(5):630-639 PMID: 3297112
74. Ouweneel et al. Impella CP Versus Intra-Aortic Balloon Pump in Acute Myocardial Infarction Complicated by Cardiogenic Shock: The IMPRESS trial. *J Am Coll Cardiol.* 2016: 23127. PMID: 27810347
75. Anderson MB et al. Benefits of a Novel Percutaneous Ventricular Assist Device for Right Heart Failure: The Prospective RECOVER RIGHT Study of the Impella RP Device. *J Heart Lung Transplant.* 2015;34(12):1549-560. PMID: 26681124
76. Slaughter MS et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med.* 2009; 361:2241. PMID: 19920051
77. Mehra MM et al. A fully magnetically levitated circulatory pump for advanced heart failure. *N Engl J Med.* 2017; 376:440-450. PMID: 27959709
78. Sheu JJ et al. Early extracorporeal membrane oxygenator-assisted primary percutaneous coronary intervention improved 30-day clinical outcomes in patients with ST-segment elevation myocardial infarction complicated with profound cardiogenic shock. *Crit Care Med.* 2010;38:1810. PMID: 20543669
79. Mancini DM et al. Value of peak exercise oxygen consumption for optimal timing of cardiac. PMID: 1999029
80. Cardiac Transplantation: Update on a road less traveled. PMID: 3190306

ARRHYTHMIAS AND ELECTROPHYSIOLOGY

Narrow Complex Tachycardias

A narrow complex tachycardia (NCT) refers to a tachycardia with QRS duration <120ms and typically implies normal electromechanical conduction from a supraventricular origin. Generally, it is helpful to organize NCTs by mechanism (automaticity, re-entry, or triggered activity) and anatomic origin (sinus node, atria, AV node).

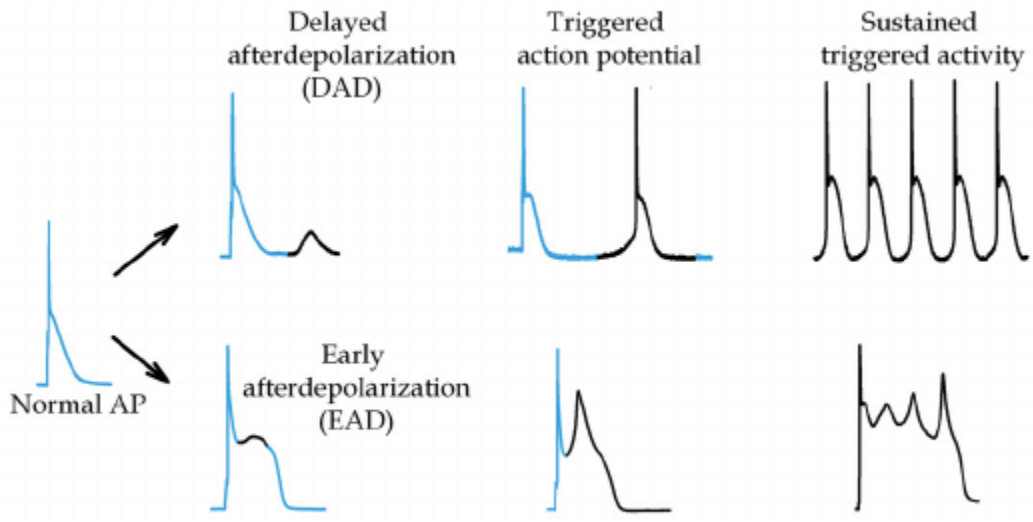
PATHOPHYSIOLOGY
Tachyarrhythmias are caused by one of three mechanisms: re-entry, automaticity, or triggered activity

1. Re-entry: most common mechanism of NCT and is thought to be the result of cyclic conduction around an electrical circuit. Reentry can occur when the following three criteria are met:
   1. There are two distinct but parallel conducting pathways connected proximally and distally
   2. One pathway must have a substantially longer refractory period than the other pathway
   3. The pathway with a shorter refractory period must conduct electrical impulses slower than the other pathway

Initiation: re-entry can be initiated when an appropriately timed premature impulse is introduced to the circuit. If a premature impulse is blocked by the longer refractory period of one limb of the circuit and preferentially conducts down the slowly conducting limb of the circuit, enough time can elapse such that the current can travel in retrograde fashion up the newly repolarized limb and reenter the circuit from the beginning, forming a continuous circuit. Re-entry can also be "set up" by scar and/or ischemia that produce areas of tissue heterogeneity (though this is more common in ventricular arrythmias).

2. Automaticity: "automatic" depolarization of electrical foci in different areas of the heart (atria, AV junction, ventricles) which may be physiologic (e.g. automatic pacemaker function of the SA resulting in normal sinus rhythm or sinus tachycardia). Abnormal automaticity at specific location(s) of the heart can trigger tachyarrhythmias (both atrial and ventricular), typically in response to metabolic insults (ischemia, hypoxemia, sympathetic tone, and electrolyte and acid-base derangements).

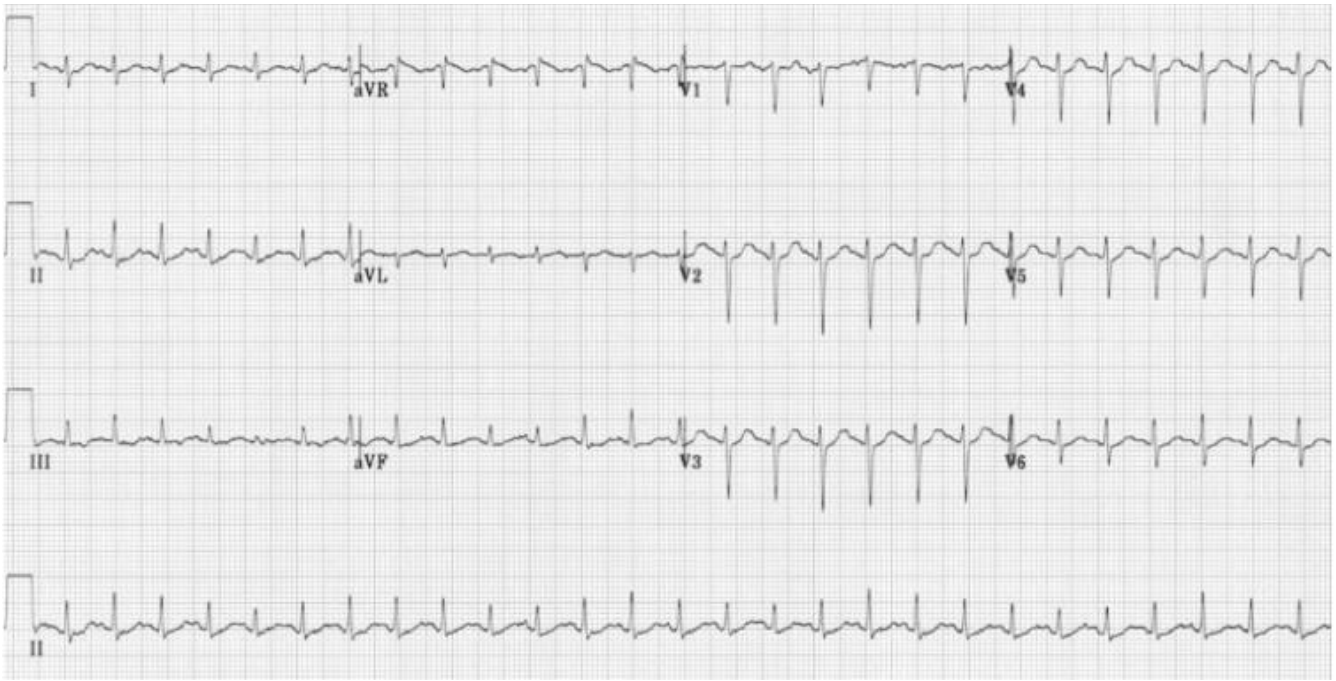
3. Triggered activity: shares features of both automaticity and re-entry and occurs when there is interruption of normal cardiac repolarization by "afterdepolarizations," early or delayed depolarizations that either proceed (early afterdepolarizations) or follow (delayed afterdepolarizations) the cardiac action potential. These spontaneous or triggered beats cause extrasystoles and lead to tachyarrhythmias. In early afterdepolarization, abnormal oscillations in the membrane potential are seen during phase 2 (plateau) and early repolarization in phase 3 (e.g. long QT syndrome, Torsades). In delayed afterdepolarization, the oscillations occur after full repolarization (e.g. digitalis toxicity due to enhanced calcium influx). Either early or delayed after depolarizations can lead to self-sustaining arrhythmic events.



Tachycardia by Site of Origin: SINUS NODE
NCTs involving the sinus node include sinus tachycardia and sinus node re-entry tachycardia.

Sinus tachycardia

- Presentation: HR 100–150 in older pts. Can be as high as 200 in young patients (max HR ~ 220-age)
  - Initiation is gradual (heart rate trend on telemetry increases over seconds)
  - P wave axis and morphology unchanged compared to baseline ECG
- Pathophysiology: most frequently secondary to other cause (physiologic) Due to an underlying process (pain, fever, hypovolemia/shock, CHF, PE, anemia, hyperthyroidism, AV fistula) or drugs (intoxication of caffeine, anticholinergics, catecholamines, nicotine, or withdrawal from EtOH, benzos, opiates). May be seen in roughly one-third of patients with acute MI (Circulation 1972;45:681)
  - Idiopathic (primary):
    - Inappropriate Sinus Tachycardia (IST) is idiopathic resting sinus tachycardia, typically with very high sinus rates on exertion
    - Paroxysmal Orthostatic Tachycardia Syndrome (POTS) is a separate diagnosis characterized by marked sinus tachycardia upon standing
    - Both IST and POTS are diagnoses of exclusion after physiologic ST is ruled out
- Treatment: physiologic treat the underlying cause
  - IST or POTS: treatment is primarily for symptoms (tachyarrhythmia-mediated cardiomyopathy is exceedingly rare). BB is the most common treatment vs less often non-dihydropyridine CCB, catheter ablation of SA node, ivabradine (off label but can be effective)



Sinus Tachycardia: https://litfl.com/sinus-tachycardia-ecg-library/

Sinus node re-entry tachycardia (SANRT)

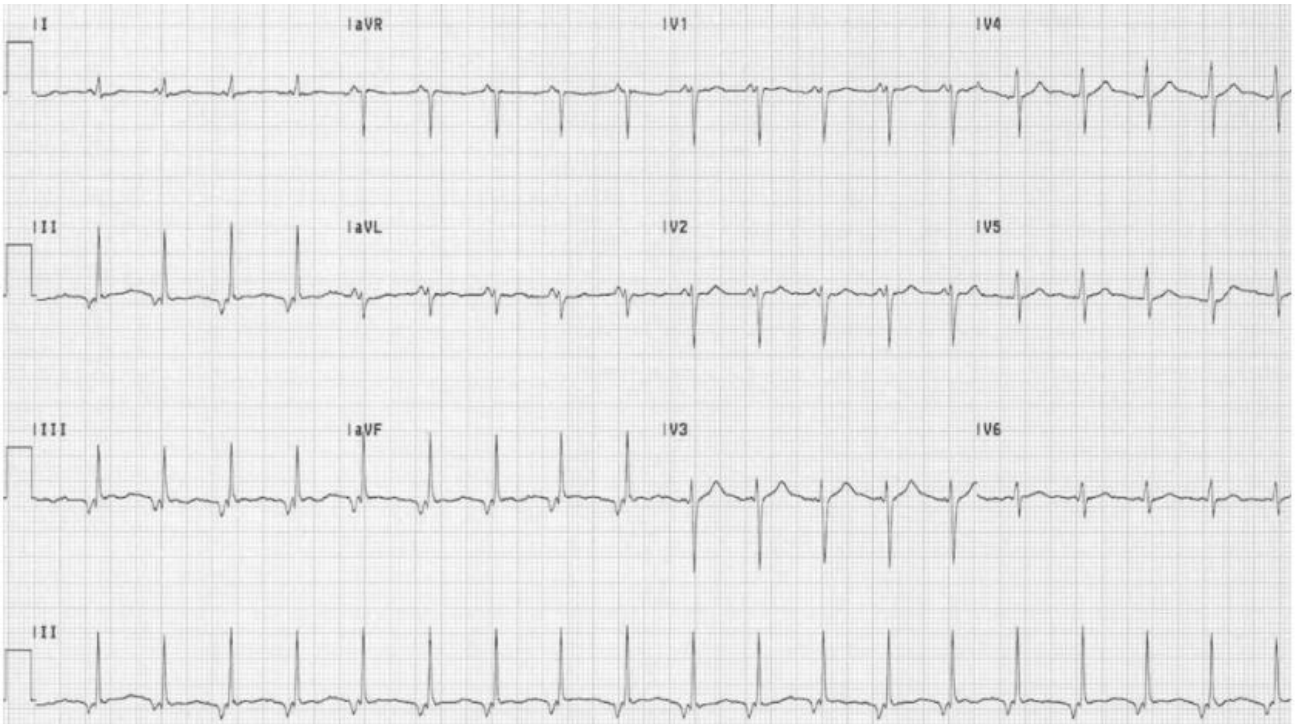
- Presentation
  - Can often occur in the presence of structural heart disease
  - Initiation and termination are abrupt (paroxysmal) and can be brought on by pacing
  - P wave axis and morphology are unchanged compared to baseline (sinus) ECG
  - There is often little that will differentiate this from sinus tachycardia on ECG and telemetry and will often require a high index of clinical suspicion and invasive EP studies for diagnosis
- Pathophysiology
  - Re-entry within or adjacent to the SA node
- Treatment
  - Acute: Vagal maneuvers, modified Valsalva (passive leg raise after Valsalva terminated SVT 43% of time vs 17% of time with Valsalva alone, Lancet 2015; 386: 1747), adenosine, rapid atrial pacing
  - Chronic: BB, non-dihydropyridine CCB and digoxin can be used to prevent recurrence (although evidence for benefit still lacking); catheter ablation

Tachycardia by Site of Origin: ATRIOVENTRICULAR NODE

These include non-reentrant junctional tachycardias, AV nodal re-entrant tachycardia (AVNRT), and AV reciprocating tachycardia (AVRT).

Junctional Tachycardia

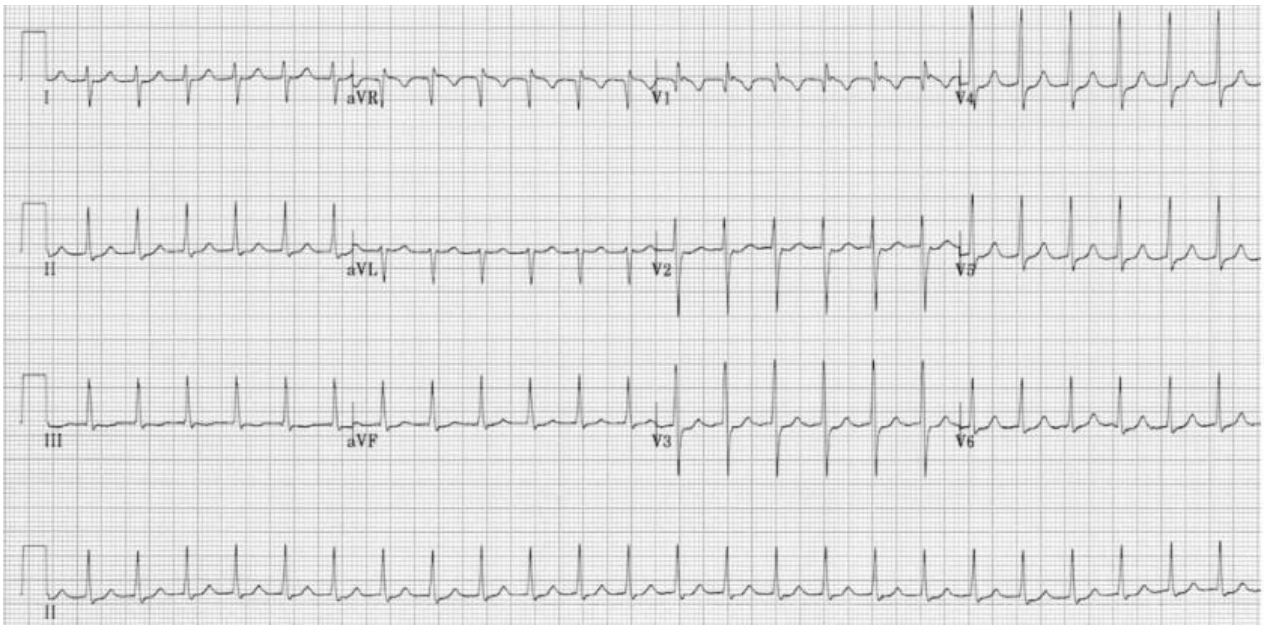
- Presentation
  - These generally include junctional ectopic tachycardia (JET) and accelerated junctional rhythm (which is known as non-paroxysmal junctional tachycardia of NPJT). Junctional tachycardias can be difficult to distinguish from other arrhythmias, particularly AVNRT. Retrograde P waves can be observed, and incomplete A-V dissociation is frequent with intermittent capture of sinus beats by the AV node leading to irregular ventricular rates that can also mimic atrial fibrillation
  - Junctional ectopic tachycardia (JET):
    - Rare and relatively benign in adults; more commonly associated with, and often incessant in infants after cardiac surgery for CHD
    - Rapid, occasionally irregular NCT, with rates typically 120 to 220
  - Non-paroxysmal junctional tachycardia(NPJT):
    - More common in adults than junctional ectopic tachycardia
    - Also referred to as accelerated junctional rhythm, rates typically 70 to 130
- Pathophysiology
  - Junctional ectopic tachycardia: Arises from an accelerated, ectopic focus in the AV junction (including the His bundle)
  - Non-paroxysmal junctional tachycardia: Most often due to digitalis toxicity (digitalis can enhance phase 4 depolarization of the His-Purkinje fibers) but also seen in acute MI
- Treatment
  - Junctional ectopic tachycardia: Acute :IV nodal blockade in the acute setting, Chronic: PO for ongoing management; ablation can be considered if symptomatic and resistant to medical therapy, but is very risky (can result in AV block)
  - Non-paroxysmal junctional tachycardia: Treatment of underlying condition (digitalis toxicity, MI)



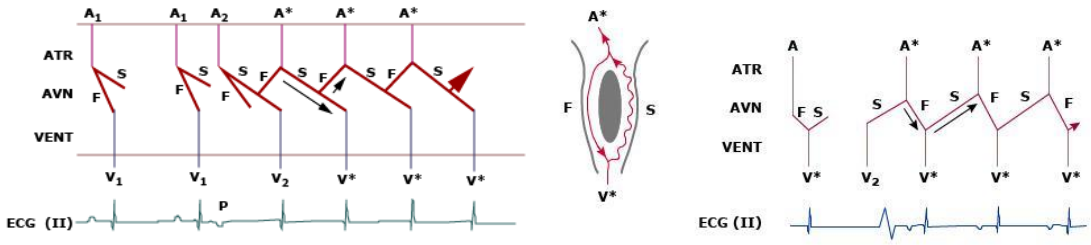
Junctional Tachycardia: https://litfl.com/accelerated-junctional-rhythm-ajr/

AV nodal re-entrant tachycardia (AVNRT)

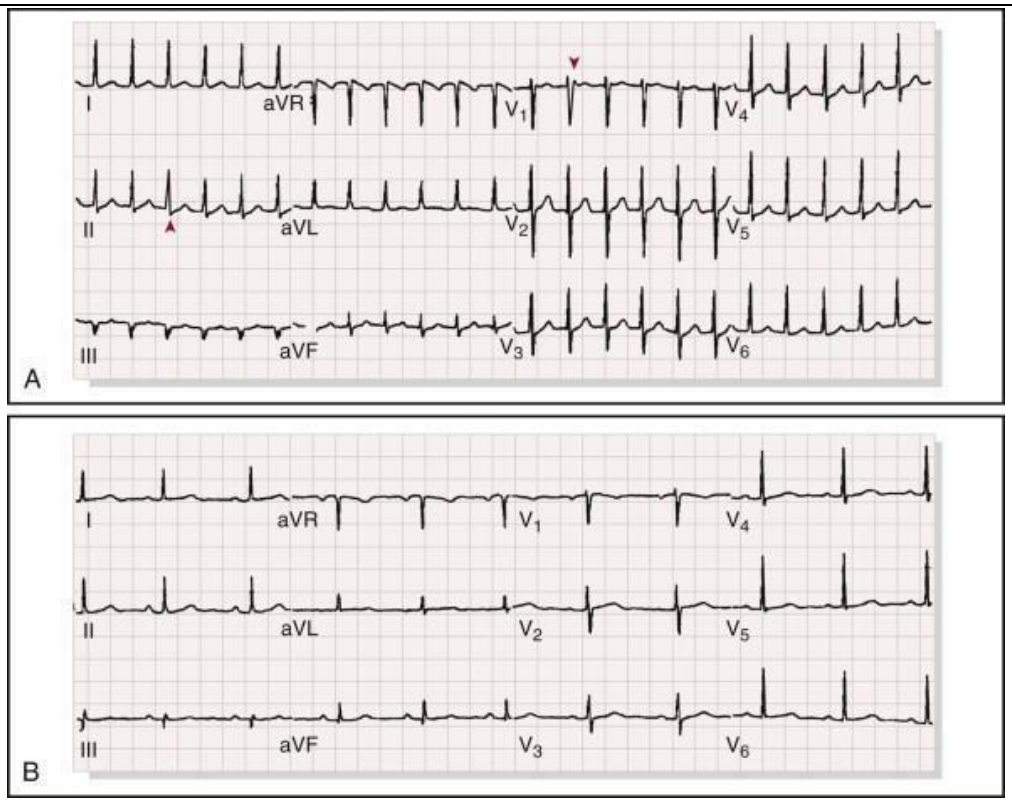
- Presentation
  - Initiated by a PAC or PVC and onset and initiation are abrupt
  - There is always a 1:1 AV relationship, generating a regular rhythm with ventricular rates typically between 150–220
  - Ps usually buried within QRS, or found immediately before or after QRS.
- Pathophysiology: re-entry circuit within the AV node with dual pathway physiology
  - Typical ("slow-fast"): Represents >90% of AVNRT in which the impulse travels antegrade down the slow pathway and retrograde up the fast pathway. This classically generates a short RP tachycardia
  - Atypical ("fast-slow", "slow-slow"): In these cases, the impulse travels initially via the fast pathway, then returns via the slow. This usually generates a long RP tachycardia
- Treatment
  - Acute: Initial management usually involves vagal maneuver and/or adenosine to terminate, but if the patient is unstable, DCCV should be attempted upfront. To increase the chance of success with vagal maneuvers, have the patient strain (e.g. blow into a syringe) in a semi-recumbent position (60 seconds) and then perform a passive leg raise (45 degrees, 60 seconds) which increases the chance of success from 17% to 43% compared to standard Valsalva (REVERT RCT in Lancet, 2015)
  - Additional effective therapies involve medications that block the AV node, such as BBs and CCBs
  - Definitive Tx involves radiofrequency catheter ablation, which has a cure rate > 95%



Typical slow-fast AVNRT: https://litfl.com/supraventricular-tachycardia-svt-ecg-library/



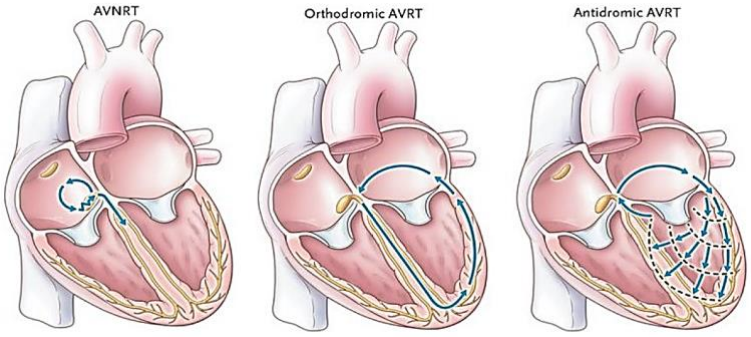
Ladder diagrams of typical (slow-fast) AVNRT (left) and atypical (fast-slow) AVNRT (right). In typical AVNRT, a PAC triggers re-entry that beings anterograde along the slow pathway (while the fast pathway is refractory). Retrograde conduction occurs along the fast pathway, generating a "short RP." In atypical AVNRT, a PVC triggers re-entry with anterograde conduction via the fast pathway and retrograde atrial depolarization via the slow pathway, generating a "long RP.". A = atrial depolarization, V = ventricular depolarization, F = fast pathway, S = slow pathway, ATR = atrium, AVN = AV node, VENT = ventricle. For more information regarding laddergrams, consider the following link and source
https://ecg-interpretation.blogspot.com/2013/06/ecg-interpretation-review-69-pvc-pjc.html



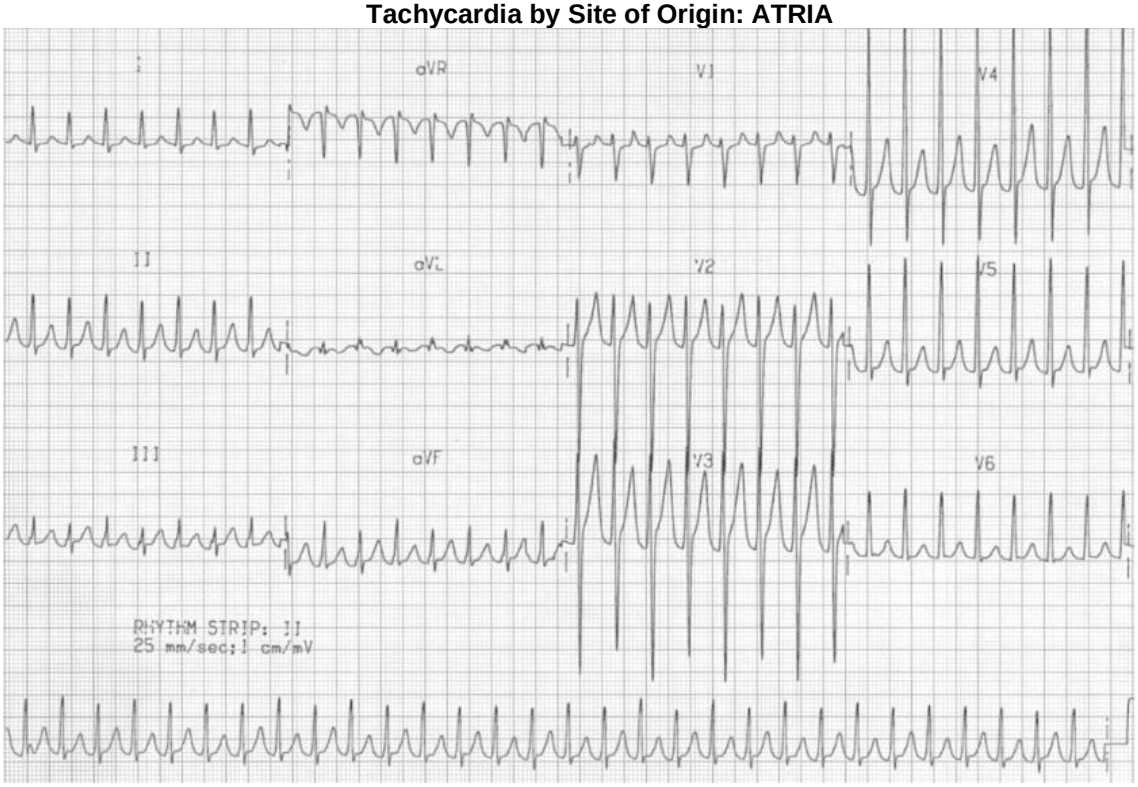
AVNRT with retrograde P forming a pseudo r' in V1 and pseudo-S in II, III, aVF (A). These are absent in NSR (B).

AV nodal reciprocating tachycardia (AVRT)

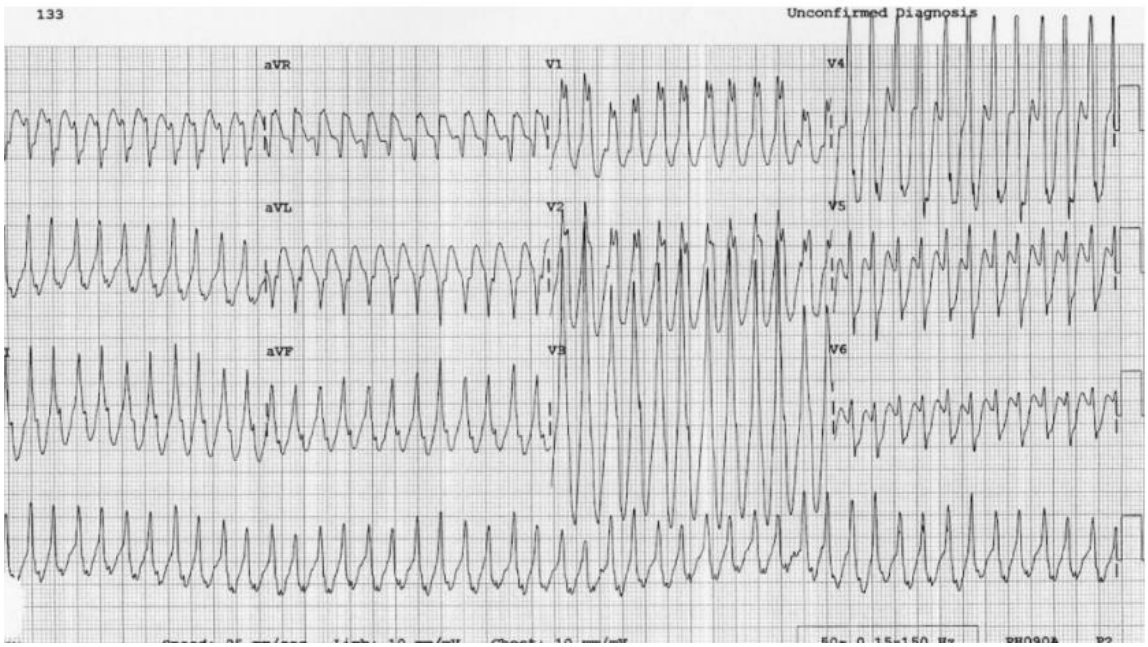
- Presentation: Similar to AVNRT in that there is a 1:1 AV relationship generating a regular rhythm but ventricular rates are often faster and P waves tend to be further separated from the QRS complex (following the QRS either on the ST segment or in the T wave)
  - In contrast to AVNRT, AVRT requires the presence of at least one accessory pathway, which may be "concealed" (i.e. normal baseline ECG) or "manifest" (i.e. evidence of accessory pathway on baseline ECG such as a delta wave in WPW)
- Pathophysiology
  - Anterograde conduction can occur via the AV node (with retrograde conduction up the accessory pathway, i.e. orthodromic AVRT) or via the accessory pathway (with retrograde conduction either through the AV node, or less commonly, via another accessory pathway, i.e. antidromic AVRT).
    - Orthodromic AVRT: More common (95%). Anterograde conduction though the AV node produces a narrow QRS complex unless there is aberrant conduction
    - Antidromic AVRT: Less common. Anterograde conduction down the accessory pathway produces a wide, maximally pre-excited QRS complex which may be mistaken for VT
- Notable case reports and discussions of variants of AVRT:
  - *Permanent junctional reentrant tachycardia* (PJRT): https://doi.org/10.1016/S0735-1097(20)33848-1 [39]
  - *Mahaim tachycardias*: https://doi.org/10.1016/j.hrcr.2021.07.012 [40]
  - *Lown-Ganong-Levine Syndrome*: https://doi.org/10.12659/ajcr.906767 [41]
- Treatment
  - Orthodromic AVRT (narrow QRS): AV nodal blockade: vagals > IV adenosine > IV verapamil, IV beta blockers including metoprolol > IV procainamide.
  - Antidromic AVRT (wide QRS): IV procainamide is the preferred option anywhere outside the EP lab. While antidromic AVRT can be treated with rate control if the diagnosis is absolutely certain, co-occurring atrial fibrillation and VT must to be excluded as nodal blockade can cause the rhythm to degenerate and acutely worsen.
  - Atrial fibrillation with preexcitation: IV procainamide > IV ibutilide. It is critical to avoid nodal blockade with adenosine, CCB's, BB's, amiodarone, and digoxin in patients with atrial fibrillation with pre-excitation because they will slow conduction through the AV node and facilitate anterograde conduction through the accessory pathway, which can lead to VF. However, a *regular rhythm effectively rules out atrial fibrillation*.
  - Acute or refractory , DCCV
  - Definitive treatment requires ablation of the accessory pathway, which carries a success rate between 85–98% depending on the pathway's location



Tachycardia by Site of Origin: ATRIA



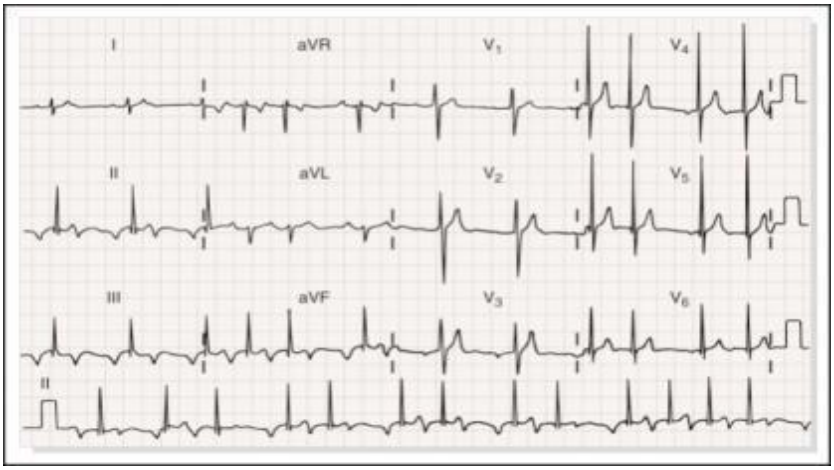
Orthodromic AVRT: https://litfl.com/atrioventricular-re-entry-tachycardia-avrt/



Antidromic AVRT: https://litfl.com/atrioventricular-re-entry-tachycardia-avrt/

Atrial tachycardia (AT)

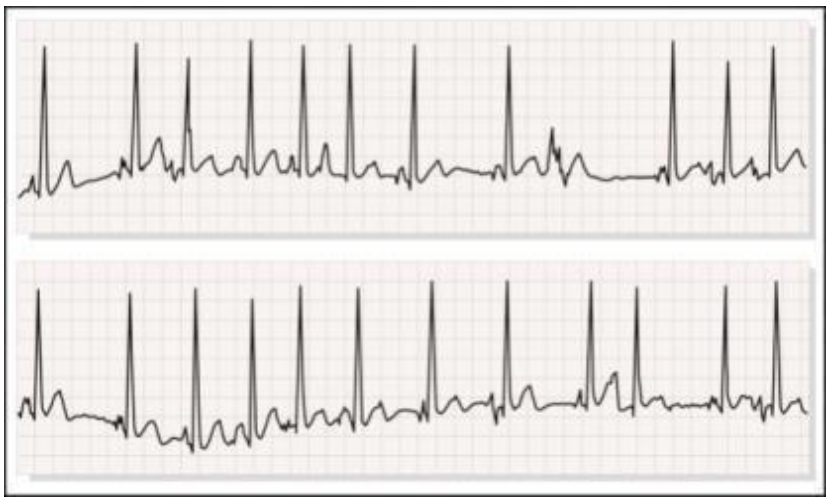
- Presentation: atrial rate 100–250. Ventricular rate typically 90–150 (due to variable block).
  - P wave morphology is different from baseline sinus P wave,
    - When AV block present, baseline between P wave is isoelectric in all leads.
- Pathophysiology: Often idiopathic in young patients. Commonly seen in structural heart disease or dig toxicity (which can be exacerbated by hypokalemia)
- Treatment: Extremely difficult to control with nodal blockade alone. Radiofrequency ablation is often required if AT is incessant, symptomatic/hemodynamically significant, and medically refractory.



AT with variable block. When P's are consecutive, RP > PR.

Multifocal Atrial tachycardia (MAT)

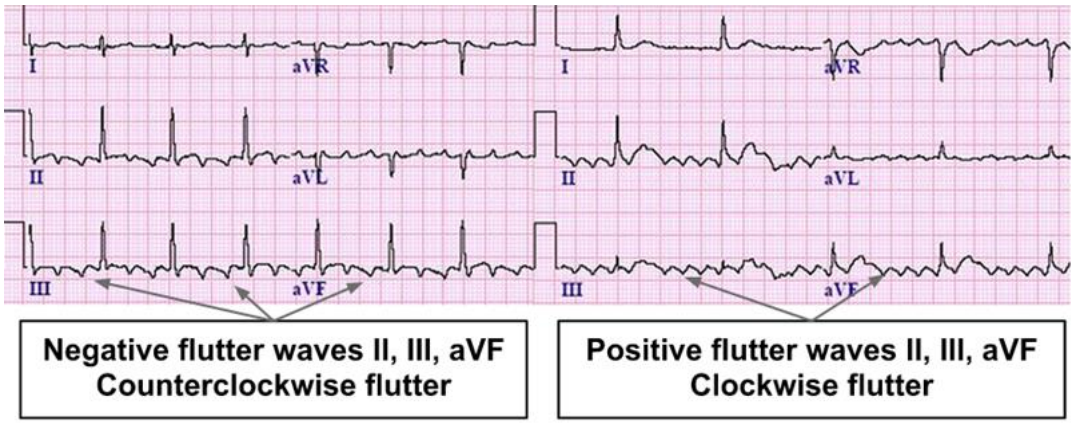
- Presentation
  - Atrial rate 100–250. Ventricular rate typically 90–150 (due to variable block).
  - 3 different P morphologies, often with varying R-P and P-R intervals
  - When AV block present, baseline between P waves is isoelectric in all leads.
- Pathophysiology*:* Seen in older patients with chronic lung disease or atrial enlargement. Often preceded or followed by atrial fibrillation/flutter, paroxysmal AT, or frequent PACs (Am Heart J 1988;115:680)
- Treatment: Can typically be monitored in the absence of decompensation. Replete both magnesium and potassium prior to medical therapy. Rate control is reported to work better than rhythm control for MAT. In the presence of cardiopulmonary disease, choose non-DHP CCB's such as verapamil > BBs. If unstable, consider DCCV or ablation.



MAT with variable Ps and PR, RP intervals.

Atrial flutter

- Presentation
  - Atrial rate 250–350, often 300. Ventricular rate can be around 150 bpm if there is 2:1 A-V conduction.
  - Typical ("CTI'"): 90% of patients have typical flutter with counterclockwise reentry around the tricuspid valve. Sawtooth "F" waves are negative in the inferior leads based on counterclockwise conduction down the right atrial anterolateral free wall, across the cavotricuspid isthmus, and more slowly up the interatrial septum
  - Atypical forms of atrial flutter also exist, with a wide variety of atrial rates and p wave morphologies. These are more common after catheter/surgical ablation of atrial fibrillation
- Pathophysiology: Macro-reentrant circuit
- Treatment:
  - If 2:1 block, can first trial vagal maneuvers. Adenosine may also be trialed and generally will transiently slow A:V conduction and the ventricular rate but will not terminate atrial flutter (6mg rapid IV push, followed by 12mg push if no response; if administered through a central line, the doses are 3mg-->6 mg).
  - Medical management: Anticoagulation and rate/rhythm control, similar to AFib
  - Always rate control first with BB, CCB, and/or digoxin before attempting rhythm control with class IA or IC agents (because these anti-arrhythmics can facilitate embolization of an atrial thrombus as well as faciliatate 1:1 ventricular conduction with rates in the 300's. Amiodarone 200mg QD can be used to prevent recurrence. DCCV can be considered if atrial flutter is associated with hypotension or decompensated heart failure. Typical flutter is most amenable to catheter ablation



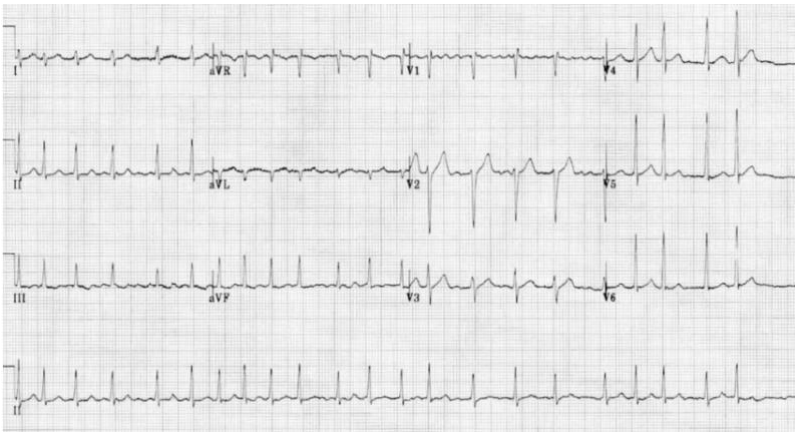
Atrial fibrillation

- Nomenclature:
  - Paroxysmal: Recurrent AF (≥ 2 episodes) that terminates spontaneously within 7 days. Episodes of AF of ≤ 48 hours duration that are terminated with electrical or pharmacologic cardioversion should also be classified as paroxysmal AF episodes.
  - Persistent: Continuous AF that is sustained beyond 7 days. Episodes in which a decision to cardiovert the patient after ≥ 48 hours of AF, but prior to 7 days, should also be classified as persistent AF episodes.
  - Long-standing persistent: Duration > 12 months; efforts to terminate, either chemically or electrically, are typically unsuccessful although catheter ablation may restore sinus rhythm in some patients.
  - Permanent: Persistent AF where further attempts at rhythm control are indefinitely deferred
- Pathophysiology: AF results from an abnormal atrial response to reentry and/or rapid focal ectopic firing. In the case of reentry, fibrillatory activity may be generated from a single localized reentry circuit or result from multiple functional reentry circuits that vary in time and space. Alternatively, there may be an ectopic focus that generates regularly firing, rapid discharges.
  - Natural history of AF may involve progression from paroxysmal to persistent to long-standing persistent forms. At the tissue level, this can result from atrial remodeling caused by the arrhythmia itself, progressive fibrosis, and worsening of underlying heart disease. AF-related electric remodeling results from altered expression and function of cardiac ion channels, which favor the development of functional reentry substrates. With AF termination, some of these changes can be reversible, a process known as reverse remodeling. If left untreated, however, the remodeling and fibrosis can progress which contribute to persistent AF.
- Management
  - Stable AF: rate versus rhythm control. If AF is self-limited, or has a potentially reversible cause, restoration of normal sinus rhythm should be pursued. Pharmacological or direct current cardioversion

(DCCV) has a higher success rate when AF has been present for less than 24 hours. Remember the adage, “AF begets AF” (through irreversible electrical remodeling).

- Studies that have examined rate control vs medical rhythm control have not detected differences in mortality or stroke rates.
- *Caveats*: these studies enrolled predominantly older patients (average age 70), most of whom had persistent AF in the setting of structural heart disease and were able to tolerate AF from a symptomatic standpoint; younger patients and those with severe symptoms from AF were underrepresented. In addition, follow-up was limited to just a few years. Thus, the results of these trials do not necessarily apply to younger patients without heart disease or those whose dependency on SR is likely to change appreciably over time.

- Unstable AF DCCV: patients with hypotension, hypoxemia, decompensated heart failure, pre-excitation, worsening ischemia, angina or decreased responsiveness often necessitate emergent DCCV, ideally preceded by sedation (usually fentanyl/midazolam or propofol depending on patient stability and coordinated by cardiac anesthesia, CCU or ER team). Alternatively, amiodarone may be used in conjunction with neo (given reflex bradycardia) in patients who are hypotensive. In addition, amiodarone may help to maintain SR after DCCV.
- Acute rate control usually achieved through AV nodal blockers (see Table 2).
  - While in the CCU/SDU, be aware of the negative inotropic effects of BB & CCB
  - In the case of atrial fibrillation in sepsis, a recent large retrospective analysis showed that IV BBs were associated with reduced hospital mortality when compared with CCBs, digoxin, and amiodarone.[8]



Atrial Fibrillation with RVR: https://litfl.com/atrial-fibrillation-ecg-library/

Table 1: Summary of Trials Examining Rate vs Rhythm Control in AF

Trial	Characteristics	Results
Pharmacological Intervention in Atrial Fibrillation[2] (PIAF) *Lancet*, 2000	-Randomized trial (N=252) -Primary endpoint: Symptom improvement -Rate control with diltiazem (N=125) vs rhythm control with DCCV+amiodarone (N=127) -F/u interval: 1 year	-No difference in primary endpoint -Rhythm control strategy demonstrated improved exercise tolerance, but hospital admissions were more frequent in this group
Atrial Fibrillation Follow-up Investigation of Rhythm Management[3] (AFFIRM) *NEJM*, 2002	-Randomized multicenter trial (N=4060) -Primary endpoint: Overall mortality -Rate control with digoxin/BB/or CCB+warfarin vs rhythm control (many different agents used) -F/u interval: 3.5 years	-No difference in primary endpoint overall -Rate control strategy demonstrated mortality reduction for patients over the age of 65 (HR 0.76) and those who did not have a history of heart failure (HR 0.69) -Rhythm control group with more hospitalizations and adverse drug effects
Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study Group[4] (RACE) *NEJM*, 2002	-Randomized trial (N=522) -Primary endpoint: Composite of CV death, admission for CHF, severe bleeding, need for PPM, or severe drug side effect -Rate control with digoxin/BB/or CCB (N=256) vs rhythm control with DCCV+anti-arrhythmic (many agents used) (N=266) -F/u interval: 2.3 years	-Rate control non-inferior to rhythm control in terms of primary endpoint
Randomized trial of rate-control versus rhythm-control in persistent atrial fibrillation[5] (STAF) *JACC*, 2003	-Randomized multicenter trial (N=200) -Primary endpoint: Composite of death, need for CPR, CVA, and systemic embolism -Rate control (N=100) vs rhythm control (N=100) -F/u interval: 1.6 years	-No difference in terms of mortality, morbidity, and quality of life -However during follow up period, only 23% of rhythm control group remained in NSR, after up to 4 DCCVs
Rate control vs rhythm control in patients with nonvalvular persistent atrial fibrillation: the results of the Polish How to Treat Chronic Atrial Fibrillation[6] (HOT CAFE) *Chest*, 2004	-Randomized multicenter trial (N=205) -Primary endpoint: Composite of all-cause mortality, number of thromboembolic events, and major bleeding -Rate control (N=101) vs rhythm control with stepwise regimen of: disopyramide, propafenone, sotalol, and amiodarone (N=104) -F/u interval: 1.7 years	-No difference in primary endpoint -Rhythm control strategy demonstrated improved exercise tolerance, but hospital admissions were more frequent in this group (74% vs 12%)
Rhythm control versus rate control for atrial fibrillation and heart failure[7] (AF-CHF) *NEJM*, 2008	-Randomized multicenter trial (N=1376) in patients with both AF and CHF -Primary endpoint: Time to death from all cardiovascular causes -Rate control (N=694) vs rhythm control (N=682) -F/u interval: 3.1 years	-Rhythm control strategy does not reduce the rate of CV death when compared to rate control -Also no difference in all-cause mortality, stroke, and worsening HF
Early Rhythm-Control Therapy in Patients with Atrial Fibrillation[36] NEJM, 2020	-Randomized multicenter trial (N=2789) -Primary endpoint: composite CV death, CVA, or hospitalization - Rhythm control vs usual care -F/u interval: 5.1 years (stopped early)	- Rhythm control strategy reduced composite of CV death, CVA, or hospitalization (HR, 0.79; P=0.005) - No statistical difference in safety outcomes between groups

Rhythm Control Strategies: Before initiating antiarrhythmic drug (AAD) therapy, treatment of precipitating or reversible causes of AF should be pursued. The goal of AAD therapy include a reduction in the frequency and duration of episodes of AF as well as an emerging goal of reducing mortality and hospitalizations associated with this condition. See Figure 1 and Table 3.

Electrical Cardioversion (See EP Procedures section for more information)

- DCCV is the most effective method of restoration of SR, and is successful at least 80% of the time.
- If the first attempt fails, a repeated shock can be delivered following the administration of an AAD (amiodarone, flecainide, ibutilide/dofetilide, propafenone or sotalol). However, if DCCV continues to fail, particularly if only able to induce short periods of SR between relapses, repeated attempts are not recommended. DCCV is relatively contraindicated in those with digitalis toxicity or hypokalemia.
- Pre-procedure anticoagulation: patients with AF of 48 hour duration or longer should be anticoagulated for at least 3 weeks prior
    - An alternative strategy is to perform TEE in search of LA thrombus. If no thrombus can be found, DCCV can be performed immediately after anticoagulation with UFH or another agent has been started. Patients are then transitioned to oral anticoagulation. In the ACUTE trial, outcomes with TEE guidance have been found to be similar to the traditional prolonged anticoagulation strategy.[9]
- Post-procedure anticoagulation: all patients should receive AC for at least 4 weeks following DCCV as risk of thromboembolism is high in the post-cardioversion period due to changes in cardiac conduction and myocardial stunning.

Chemical Cardioversion and Maintenance of SR therapy

- In general, chemical cardioversion is less effective than DCCV. The success is significantly higher for acute (< 7 days) compared with longer-duration AF. Moreover, drug-induced torsades de pointes and other serious arrhythmias may result when using AADs for cardioversion. If desired, flecainide, propafenone or ibutilide are the recommended agents, see table 3 for further details.

Catheter Ablation - Trials

- AATAC (2016): In patients with symptomatic (NYHA II-III) heart failure with reduced ejection fraction (HFrEF, LVEF ≤40%) and persistent atrial fibrillation (AF) chosen for a rhythm control strategy, AF ablation was associated with a 36% absolute increase in AF-free survival at 24 months. There was also a 26% absolute reduction in unplanned hospitalizations and a 10% absolute reduction in overall mortality with AF ablation.[10]
- FIRE AND ICE (2016): In patients with symptomatic paroxysmal atrial fibrillation (pAF) resistant to antiarrhythmic drugs referred for pulmonary vein isolation (PVI), balloon cryoablation is noninferior to radiofrequency ablation in regards to a primary outcome of composite clinical failure (recurrent AF, prescription of antiarrhythmic drugs, or repeat ablation) more than 90 days after the index procedure.[11]
- CASTLE-AF (2018): In patients with AF and symptomatic (NYHA II-IV) systolic heart failure (LVEF ≤ 35%), catheter ablation is associated with a 16.1% absolute reduction in death or hospitalization for heart failure when compared to medical therapy (rate or rhythm control). This difference was driven both by a 11.6% absolute reduction in death and a 15.2% absolute reduction in hospitalization for heart failure. Catheter ablation was also associated with greater improvement in LVEF and long-term maintenance of sinus rhythm.[12]
- CABANA (2019): In patients with atrial fibrillation (AF) requiring treatment, catheter ablation was not associated with a significant reduction in death, disabling stroke, serious bleeding, or cardiac arrest when compared to medical therapy at 12 months. The results of this trial were incorporated in the AHA/ACC 2019 AF guidelines and as a result AF ablation in patients without systolic heart failure is likely to remain an elective procedure performed with the primary purpose of symptom relief in patients who have failed, are intolerant of, or decline anti-arrhythmic therapy.[13]
- EAST-AFNET4 (2020): In patients recently diagnosed with AF (~1month) rhythm control was superior to usual care and the trial was stopped early, because the primary-outcome composite (CV death, CVA, or hospitalization) was significantly lower in the rhythm control group. While rhythm control was mostly with AAD, about 8% of participants underwent catheter ablation by 1 year and 20% by 2 years. This trial has not dramatically altered guidelines as of yet, but its findings alongside those from CABANA and CASTLE-AF suggest that normal sinus rhythm matters.[36]

Table 2: IV and Oral Agents for HR control in AF

Drug	LOE	Loading Dose	Onset	Maintenance Dose	Major Side Effects
Esmolol*	I-C	500 mcg/kg IV over 1 min	5 min	60–200 mcg/kg/min IV	↓ BP/HR; HB; asthma, HF
Metoprolol*	I-C	2.5–5 mg IV over 2 min; up to 3 doses	5 min	NA	↓ BP/HR; HB; asthma, HF
Propranolol*	I-C	0.15 mg/kg IV	5 min	NA	↓ BP/HR; HB; asthma, HF
Diltiazem*	I-B	0.25 mg/kg IV over 2 min	2-7min	5–15 mg/h IV	↓ BP; HB, HF
Verapamil*	I-B	0.075–0.15 mg/kg IV over 2 min	3-5min	NA	↓ BP; HB, HF
Amiodarone^	IIa/C	150mg IV over 10 min	Days	0.5–1 mg/min IV	↓BP; HB, pulmonary toxicity, skin discoloration, hypo-/hyperthyroidism, corneal deposition, optic neuropathy, warfarin interaction, sinus bradycardia
Digoxin*^	I-B	1.5 mg load: 0.25 mg IV q2 x 6 OR 0.75 mg IV + 0.375 Q6H	60+ min	0.125–0.375 mg daily IV/PO	Digitalis toxicity, HB, ↓ HR

LOE: Level of evidence. *Avoid in patients with known or suspected accessory pathway. ^Useful in patients with concomitant HF.

Figure 1: Choice of Antiarrhythmic Drug (AAD) Based on Cardiovascular Comorbidities

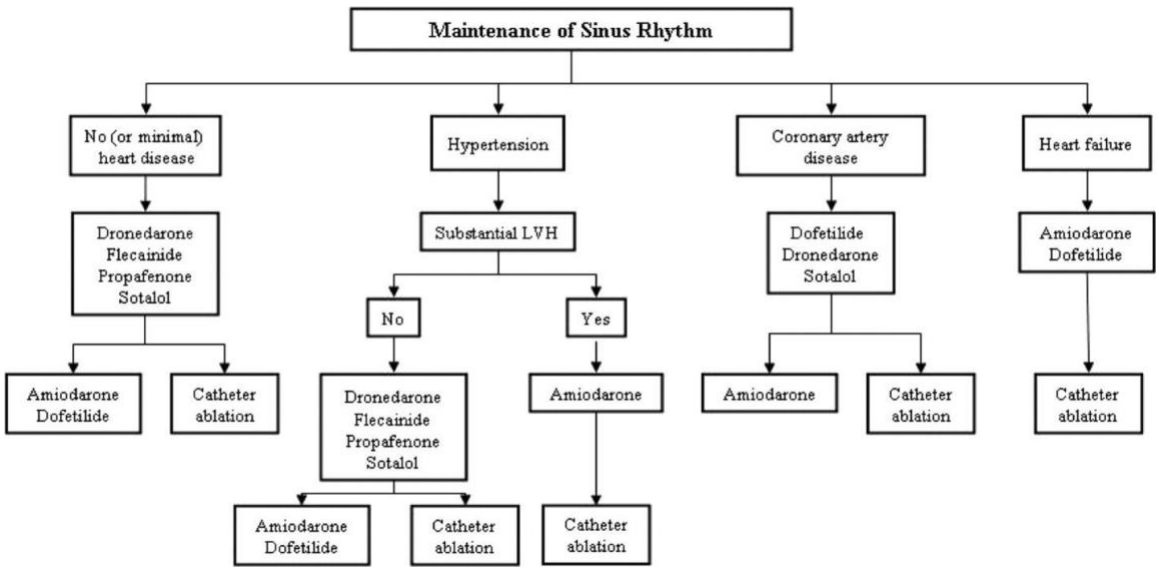


Table 3: Agents maintenance of SR

Agents for Conversion to SR (please refer to pharmacy for institutional dosing protocols)	
Ibutilide	An intravenous IKr blocker that also enhances the late inward sodium current is ~50% effective at restoring SR. It is slightly more effective for AFL than for AF. When used, patients need to be monitored closely for QT prolongation and TdP for at least 2 hours after infusionIncreases success rate of cardioversion and prevents relapses by suppressing atrial ectopy, however high incidence of potentially severe extracardiac side effects limits its use and makes it second-line or last-resort agent in non-critically ill patients.
Flecainide	A high dose of flecainide (200–300mg) can be used as an outpatient strategy once treatment has proven safe in-hospital for selected patients without sinus or AV node dysfunction, BBB, QT-interval prolongation, Brugada syndrome or structural heart disease. The overall rate of conversion tends to be >85%. Before these agents are initiated, a BB or CCB should be given to prevent atrial flutter with 1:1 ventricular conduction.
Propafenone	Most useful in paroxysmal afib and can be used in a style similar to flecanide as a pill in the pocket outpatient strategy. Avoid in those with ischemic heart disease or LV dysfunction as can be pro-arrhythmic. Before this agent is initiated, a BB or CCB should be given to prevent atrial flutter with 1:1 ventricular conduction.
Maintenance Daily Dose (OR vs. control of maintaining SR after AF conversion, # of trials)	
Amiodarone 100–400 mg (6.8, 2 trials)	More effective than class I drugs, sotalol or placebo in the long-term maintenance of SR in paroxysmal or persistent AF refractory to other drugs. Drug of choice in patients with LVH, HF, CAD or prior MI since associated with low risk of pro-arrhythmia. Also effective for HR control (BB properties). Increases success rate of cardioversion and prevents relapses by suppressing atrial ectopy, however high incidence of potentially severe extracardiac side effects limits its use and makes it second-line or last-resort agent in non-critically ill patients.
Flecainide 100–300 mg (4.3, 3 trials)	Effective in postponing the first recurrence of AF and overall time spent in AF. Limited to patients with no structural (LV dysfunction) or ischemic heart disease. Adverse effects include VT, HF and conversion to AFL with RVR.
Propafenone 450–900 mg (3.0, 4 trials)	Useful to prevent first recurrence of AF and post-DCCV. Avoid in those with ischemic heart disease or LV dysfunction as can be pro-arrhythmic.
Disopyramide 400–750 mg (2.9, 2 trials)	Prevents recurrent AF after DCCV. Considered first-line therapy in vagally induced AF; has negative inotropic and dromotropic effects that may cause HF or AV block; this negative inotropic effect may be desirable in HCM associated with dynamic outflow tract obstruction. Associated with TdP.
Sotalol 160–320 mg (2.5, 4 trials)	Not effective for chemical cardioversion but useful to prevent AF. Min effective dose is 160mg daily. Avoid in patients with asthma, HF, renal failure or prolonged QT. Requires inpatient initiation of therapy.
Dofetilide 500–1000 mcg	Useful for chemical cardioversion and maintenance of SR. Can be used in structural heart disease/CHF. Due to risk of pro-arrhythmia (QT prolongation), it must be started as inpatient, titrate to renal function.
Dronedarone 800 mg	Prolongs time to recurrence of AF. Decreases hospitalization rates. Not useful for chemical cardioversion or improving success of DCCV. Less efficacious than amiodarone but better tolerated. Associated with a significant reduction in the risk of stroke. Avoid in class IV or recently decompensated HF, particularly if depressed LV function (< 35%). Associated with increased mortality in patients with CHF or permanent AF.

Anticoagulation: General Considerations

All patients with AF should be on anticoagulation except those at the lowest risk of thromboembolic stroke. Risk is greatly increased by personal history. The CHA2DS2VASc risk score is a useful tool for assessing ischemic stroke risk in patients with AF. Note that the AHA/ACC 2019 guidelines for atrial fibrillation recommend that NOACs – including dabigatran, rivaroxaban, apixaban and edoxaban – are now the preferred recommended drug class over warfarin to reduce stroke risk

in appropriate AFib patients in men with a CHA2DS2VASc of 2 or more and 3 or more in women. In men with a CHA2DS2VASc of 1 and women with a score of 2, the decision to initiate oral anticoagulation depends on if the extra point is conferred by age 65-74 as this is the strongest risk factor. Female gender alone does not confer significantly extra risk for embolic stroke in the absence of other risk factors and does not necessitate anticoagulation by itself. Patients who have moderate-to-severe mitral stenosis or a mechanical heart valve should continue to be anticoagulated with warfarin.[1]

Anticoagulation: Specific Agents

Agent	Commentary
Warfarin	Warfarin therapy should be targeted to an INR 2–3, as measured weekly during initiation of therapy and monthly thereafter. On average, warfarin provides an annual reduction of 68% in relative risk for stroke.
Dabigatran	Approved as an alternative to warfarin for non-valvular AF, with superiority in the prevention of stroke compared to warfarin in the RE-LY trial.[15] Pro-drug, rapidly converted to active direct thrombin inhibitor. It is administered in fixed doses without laboratory monitoring of anticoagulation intensity. At a dose of 150 mg bid, it reduced the rate of stroke by 34% with no increase in major bleeding when compared to warfarin. For those with CrCl 15–30, a dose of 75 mg bid was also approved (dabigatran is not indicated for patients with CrCl < 15).
Rivaroxaban	A direct-thrombin inhibitor. In ROCKET-AF trial, it proved to be non-inferior to warfarin for the prevention of stroke and systemic embolism, with no difference in risk of major bleeding although ICH and fatal bleeding occurred less frequently with rivaroxaban.[16] It is administered at a dose of 20 mg daily, with dose reduction to 15 mg if renal impairment.
Apixaban	A direct-thrombin inhibitor, found to be superior to warfarin in preventing stroke or systemic embolism in the ARISTOTLE trial. It also caused less bleeding and lower mortality.[17] It is administered at a dose of 5 mg BID, or 2.5 mg BID if any two of the following: Age ≥ 80 years old, body weight ≤ 60 kg, serum Cr ≥ 1.5. In the AVERROES trial in patients with AF thought to be unsuitable candidates for anticoagulation with VKA, Apixaban reduced the risk of stroke without increasing the risk of major bleeding compared to aspirin.[18]
Edoxaban	A direct-thrombin inhibitor, found to be equal in efficacy to warfarin in preventing stroke or systemic embolism in ENGAGE AF-TIMI 48. It caused less bleeding.[19] It was also noted to be non-inferior to warfarin in atrial fibrillation following TAVR, but with more bleeding in the ENVISAGE-TAVI AF trial in 2021.[42] It is administered at a dose of 60 mg daily (or 30 mg daily for CrCl 15-50mL/min). Edoxaban is currently less commonly used given more frequent clinical experience with rivaroxaban and apixaban as well as equivalence rather than superiority to warfarin.
Aspirin	A poor substitute for anticoagulation, though perhaps a plausible alternative in a very low-risk patient (i.e., CHA2DS2-Vasc = 1) or one at very high risk of bleeding. The relative risk reduction for stroke is variable, but perhaps around 20%.

Anticoagulation: Special Considerations for Patients Post-PCI

Up to 1 in 10 patients undergoing PCI have AF, and in general, the literature is in the early stages of understanding optimal anticoagulation in these cases. The WOEST trial found that in patients on oral anticoagulation undergoing PCI, use of clopidogrel + warfarin (double therapy) was associated with reduction in bleeding complications as well as lower combined secondary endpoints (death, MI, revascularization, stroke, stent thrombosis) when compared to the use of clopidogrel + warfarin + ASA (triple therapy).[20] Since the publication of WOEST, the ACC/AHA guidelines suggest that patients with nonvalvular AF undergoing PCI be maintained on oral anticoagulation and clopidogrel without aspirin.[14] There is increasing evidence supporting the use of DOACs in patients with AF (RE-LY, ARISTOTLE, ROCKET AF).[15-17] A more recent study, PIONEER AF-PCI, assessed the use of DOACs in patients with nonvalvular AF undergoing PCI with stent placement and found that low-dose rivaroxaban plus either single or dual antiplatelet therapy reduces the risk of bleeding when compared to warfarin + DAPT at 1 year post-procedure without having a significant effect on the rate of major adverse cardiovascular events.[21] Note that the doses of rivaroxaban (15 mg daily or 2.5 mg BID) used in this trial are not FDA approved for AF or ACS and the results of this trial are preliminary with further trials now ongoing.

Patient with Contraindications to AC: Percutaneous and Surgical Left Atrial Appendage (LAA) Closure

- LAA closure has emerged as a mechanical alternative to pharmacologic stroke prevention in patients with a contraindication to anticoagulation. There are multiple LAA occlusion devices, including the WATCHMAN, Amulet, WaveCrest, and LARIAT system devices (Amulet and WaveCrest are currently investigational in the U.S.).

- PROTECT-AF trial: showed that percutaneous LAA closure with the WATCHMAN device was non-inferior to warfarin for the prevention of the composite endpoint of ischemic stroke, hemorrhagic stroke, cardiovascular death, and systemic embolism.[22] The PREVAIL Trial subsequently found that LAA occlusion was non-inferior to warfarin for ischemic stroke prevention, although non-inferiority was not achieved for the overall efficacy endpoint (stroke, systemic embolism, and cardiovascular/unexplained death).[23]
- Based on PROTECT & PREVAIL, the WATCHMAN device was approved by the in March 2015 for patients with nonvalvular AF for whom long-term anticoagulation is indicated but who have a contraindication.
    - After placement of an LAA occlusion device, patients are treated with oral anticoagulation + ASA for 6 weeks, followed (if successful LAA closure is documented by TEE at 6 weeks post-implant) by clopidogrel + ASA for 6 months, followed by ASA for life. Patients with absolute contraindication to oral anticoagulants are given DAPT for 6 months.
- In the LAAOS III trial, investigators were able to conclude that surgical occlusion of the LAA in patients with atrial fibrillation undergoing cardiac surgery and who went on to be anticoagulated had a lower risk of stroke than those who did not.[43]

Other Special Considerations in AF

- *Post-MI AF*: incidence of AF after AMI varies between 10–20% at 30 days. It is more common in older patients with higher Killip class (more severe AMI) and more severe LV dysfunction. Post-MI AF is associated with higher 30 day mortality compared to NSR (29.3% vs. 19%). Stroke rates are also higher in this population. Management includes urgent DCCV if RVR produces intractable ischemia or instability. IV beta-blockers are also indicated if stable.
- *AF and Pre-Excitation (WPW)*:
    - As a general rule, IV beta-blockers, CCB, digitalis, and adenosine are contraindicated, as they can facilitate anterograde conduction through the accessory pathway and result in acceleration of the ventricular rate, hypotension or VF.
    - For hemodynamically stable: a class IA antiarrhythmic IV (typically procainamide) or amiodarone
- *"Reversible" AF*: Guidelines have proposed that AF can occur as an isolated event due to a reversible stressor (e.g., thyrotoxicosis, infection, MI, cardiac surgery).
    - In the Framingham cohort, 62% of patients with an isolated episode of AF due to a "reversible" cause had recurrent AF at 15 years.[24] Overall stroke risk and mortality were similar in groups with and without a reversible stressor
    - Given higher risk for recurrent AF and elevated stroke risk, AC should be considered. However, more research is still needed here.
- *AF after Cardiac Surgery*: This is a relatively common post-surgical complication, with an incidence of 20-50%. A recent study found that there was no difference between rate and rhythm control in regards to total number of hospital days, rates of death, and serious adverse events such as thromboembolism or bleeding. At 60 days after AF onset, both patients receiving rate and those receiving rhythm control had similarly low rates of persistent AF.[25]
- *AF and Heart Failure*: The 2016 Ablation versus Amiodarone for Treatment of persistent Atrial fibrillation in patients with congestive heart failure and an implanted device (AATAC) trial evaluated the efficacy of AF ablation versus amiodarone in patients with symptomatic HFrEF and persistent AF. At 2 years, ablation was associated with a 36% absolute increase in AF-free survival compared to amiodarone. Patients receiving AF ablation also experienced a 26% absolute reduction in unplanned hospitalizations and 10% absolute reduction in overall mortality.
    - AATAC trial suggests that among patients with HFrEF and AF, AF ablation is potentially superior to amiodarone as a method for achieving and maintaining sinus rhythm in terms of AF-free survival as well as in regards to cardiovascular outcomes and mortality.[26]

References:

1. Aliot, Etienne M., et al. "ACC/AHA/ESC Practice Guidelines." *Circulation* 108 (2003): 1871-1909
2. Robert O., Bonow, Douglas Mann and Peter Libby. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine.* 9th. Singl Volume. Philadelphia: Saunders, 2011. Print
3. Delacrétaz, Etienne. "Supraventricular tachycardia." *New England Journal of Medicine* 354.10 (2006): 1039-1051
4. Griffin, Brian P et al. *Manual Of Cardiovascular Medicine*. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2013. Print
5. Spector, Peter, et al. "Meta-analysis of ablation of atrial flutter and supraventricular tachycardia." *The American journal of cardiology* 104.5 (2009): 671-677.
6. Fox, David J., et al. "Supraventricular tachycardia: diagnosis and management." *Mayo Clinic Proceedings*. Vol. 83. No. 12. Elsevier, 2008
7. Appelboam, Andrew, et al. "Postural modification to the standard Valsalva manoeuvre for emergency treatment of supraventricular tachycardias (REVERT): a randomised controlled trial." *The Lancet* 386.10005 (2015): 1747-1753.
8. Page, Richard L., et al. "2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* 67.13 (2016): e27-e115
9. Fogoros, Richard N. *Electrophysiologic Testing*. Chichester: Wiley-Blackwell, 2012. Print.
10. January, Craig T., et al. "2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* 64.21 (2014): e1-e76
11. Hohnloser, Stefan H., et al. "Rhythm or rate control in atrial fibrillation—Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial." *The Lancet* 356.9244 (2000): 1789-1794
12. Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. "A comparison of rate control and rhythm control in patients with atrial fibrillation." *New England Journal of Medicine* 347.23 (2002): 1825-1833
13. Van Gelder, I. C. "Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study Group. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation." *N Engl J Med* 347 (2002): 1834-1840
14. Carlsson, Jörg, et al. "Randomized trial of rate-control versus rhythm-control in persistent atrial fibrillation." *Journal of the American College of Cardiology* 41.10 (2003): 1690
15. Opolski, Grzegorz, et al. "Rate control vs rhythm control in patients with nonvalvular persistent atrial fibrillation: the results of the Polish How to Treat Chronic Atrial Fibrillation (HOT CAFE) Study." *Chest* 126.2 (2004): 476-486
16. Roy, Denis, et al. "Rhythm control versus rate control for atrial fibrillation and heart failure." *New England Journal of Medicine*358.25 (2008): 2667-2677
17. Walkey, Allan J., et al. "Practice patterns and outcomes of treatments for atrial fibrillation during sepsis: a propensity-matched cohort study." *Chest* 149.1 (2016): 74-83
18. Klein, Allan L., et al. "Use of transesophageal echocardiography to guide cardioversion in patients with atrial fibrillation." *New England Journal of Medicine* 344.19 (2001): 1411-1420
19. Di Biase, Luigi, et al. "Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial." *Circulation* 133.17 (2016): 1637-1644
20. Kuck, Karl-Heinz, et al. "Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation." *New England Journal of Medicine* 374.23 (2016): 2235-2245
21. Marrouche, Nassir F., et al. "Catheter ablation for atrial fibrillation with heart failure." *New England Journal of Medicine*378.5 (2018): 417-427
22. Mark, Daniel B., et al. "Effect of catheter ablation vs medical therapy on quality of life among patients with atrial fibrillation: the CABANA randomized clinical trial." *JAMA* (2019)
23. January, Craig T., et al. "2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the american college of Cardiology/American heart association task force on clinical practice guidelines and the heart rhythm society." *Journal of the American College of Cardiology* (2019): 25873
24. Connolly, Stuart J., et al. "Dabigatran versus warfarin in patients with atrial fibrillation." *New England Journal of Medicine* 361.12 (2009): 1139-1151
25. Patel, Manesh R., et al. "Rivaroxaban versus warfarin in nonvalvular atrial fibrillation." *New England Journal of Medicine* 365.10 (2011): 883-891
26. Granger, Christopher B., et al. "Apixaban versus warfarin in patients with atrial fibrillation." *New England Journal of Medicine* 365.11 (2011): 981-992
27. Connolly, Stuart J., et al. "Apixaban in patients with atrial fibrillation." *New England Journal of Medicine* 364.9 (2011): 806-817

28. Giugliano, Robert P., et al. "Edoxaban versus warfarin in patients with atrial fibrillation." *New England Journal of Medicine* 369.22 (2013): 2093-2104
29. Dewilde, Willem JM, et al. "Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial." *The Lancet* 381.9872 (2013): 1107-1115
30. Gibson, C. Michael, et al. "Prevention of bleeding in patients with atrial fibrillation undergoing PCI." *New England Journal of Medicine* 375.25 (2016): 2423-2434
31. Reddy, Vivek Y., et al. "Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial." *Jama* 312.19 (2014): 1988-1998
32. Holmes, David R., et al. "Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial." *Journal of the American College of Cardiology* 64.1 (2014): 1-12
33. Lubitz, Steven A., et al. "Long-term outcomes of secondary atrial fibrillation in the community: the Framingham Heart Study." *Circulation* 131.19 (2015): 1648-1655
34. Gillinov, A. Marc, et al. "Rate control versus rhythm control for atrial fibrillation after cardiac surgery." *New England Journal of Medicine* 374.20 (2016): 1911-1921
35. Di Biase, Luigi, et al. "Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial." *Circulation* 133.17 (2016): 1637-1644
36. Kirchhof, Pauls, Camm A. John, et al. “Early Rhythm-Control Therapy in Patients with Atrial Fibrillation.” *New England Journal of Medicine* 383 (2020):1305-1316
37. Sedej, Simon & Pieske, Burkert. (2012). Mechanisms of Ca2+-Triggered Arrhythmias. 10.5772/25906.0
38. Link MS. Clinical practice. Evaluation and initial treatment of supraventricular tachycardia. N Engl J Med. 2012;376:1438–48.’
39. Patel S, Patel A, Olshansky B, et al. TACH-ING AWAY: PERMANENT JUNCTIONAL RECIPROCATING TACHYCARDIA. J Am Coll Cardiol. 2020 Mar, 75 (11_Supplement_1) 3221.
40. Mahaim-mediated tachycardia using at times the atrioventricular node and other times a left lateral accessory pathway. Vali, Zakariyya et al. HeartRhythm Case Reports, Volume 7, Issue 10, 641 – 649.
41. Hunter, J., Tsounias, E., Cogan, J., & Young, M. L. (2018). A Case of Lown-Ganong-Levine Syndrome: Due to an Accessory Pathway of James Fibers or Enhanced Atrioventricular Nodal Conduction (EAVNC)?. *The American journal of case reports*, *19*, 309–313.
42. Van Mieghem NM, Unverdorben M, Hengstenberg C, et al. Edoxaban versus vitamin K antagonist for atrial fibrillation after TAVR. N Engl J Med. 2021.
43. Whitlock RP, Belley-Cote EP, Paparella D, et al. Left atrial appendage occlusion during cardiac surgery to prevent stroke. N Engl J Med 2021;384:2081-2091.

Wide Complex Tachycardias

A wide complex tachycardia (WCT) refers to a tachycardia with QRS duration QRS ≥ 120ms. Generally, the approach to WCT is to *assume it is a ventricular tachycardia (VT) until proven otherwise.* VT is the most common and most malignant of the WCTs, however a broader differential should be considered.

Differential Diagnosis of WCT:

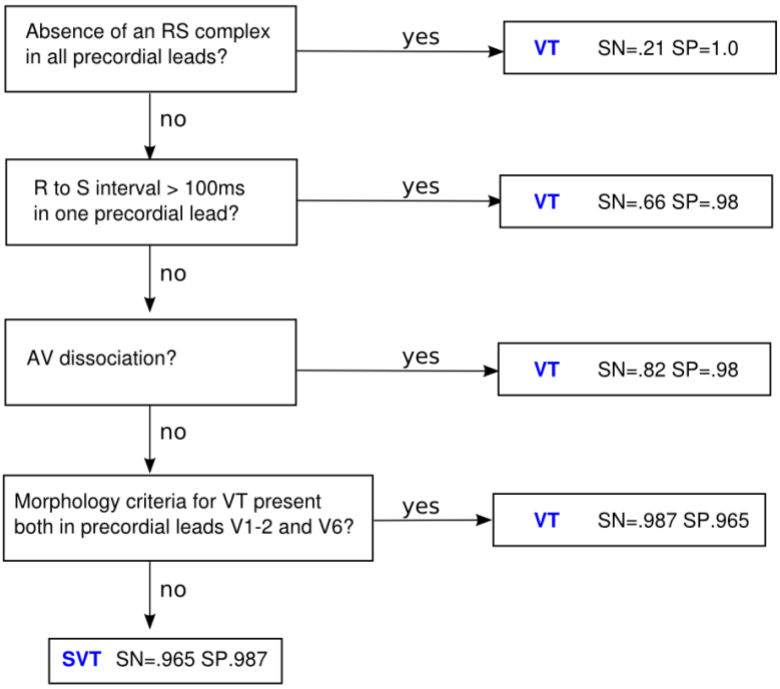
- Ventricular Tachycardia(70% of the time): ectopic or reentrant ventricular impulse spreads electrical activity slowly through the ventricular myocytes and produces a wide QRS. It originates below or very rarely at the bundle of His.
  - Monomorphic VT: has a variety of etiologies (infarct/scar being a common one)
  - Polymorphic in the setting of a normal QTc (<500 ms) is often due to ischemia
- Supraventricular Tachycardia (SVT) with Aberrancy(30% of the time): SVT (e.g. AT, AF) conducts an electrical impulse into the ventricles along the standard His-Purkinje system, but is slowed along that path as a result of:
  - Pre-existing or rate-related aberrant intraventricular conduction (e.g. bundle-branch block)
  - Drugs (e.g. class 1C anti-arrhythmics, digoxin), electrolyte abnormalities (e.g. hyperkalemia), or ischemia
  - Slowing of electrical conduction through the ventricles results in wide complex QRS
- Supraventricular Tachycardia with Pre-excitation: SVT conducts an electrical impulse into the ventricles through an aberrant conduction pathway in which depolarization advances slowly through the ventricular myocytes rather than quickly along the His-Purkinje system (for example, an underlying RBBB)
- Pacemaker-Related Tachycardia
  - Pacemaker-*mediated* tachycardia: "Endless loop" tachycardia in which the aberrant circuit is generated by the pacemaker
    - Electricity arising from the ventricular pacing lead conducts retrograde (typically, through the AV node) to the atria, producing atrial depolarization (seen as a retrograde P wave)
    - The atrial depolarization is sequentially recognized by the pacemaker, leading to atrial-sensed ventricular pacing
    - Another ventricular depolarization can conduct in retrograde fashion again through the AV node and produce a circuit
  - Pacemaker-*tracked* tachycardia: SVT is tracked by the pacemaker
    - SVT is sensed by the pacemaker, producing a wide complex beat.
      (This rhythm is less common now that devices have become sophisticated at mode switching to non-tracking modes such as VVI or DDI when the algorithm recognizes SVT or AF
  - *Note: Both pacemaker-tracked and pacemaker-mediated tachycardia can be terminated by the application of a magnet to the pacemaker, which changes the pacing mode to an asynchronous mode (VOO or DOO). This is not true for most ICDs, in which the magnet will temporarily disable ICD therapy, but will not alter the pacing mode.

ECG diagnosis of WCT

Quick reference:

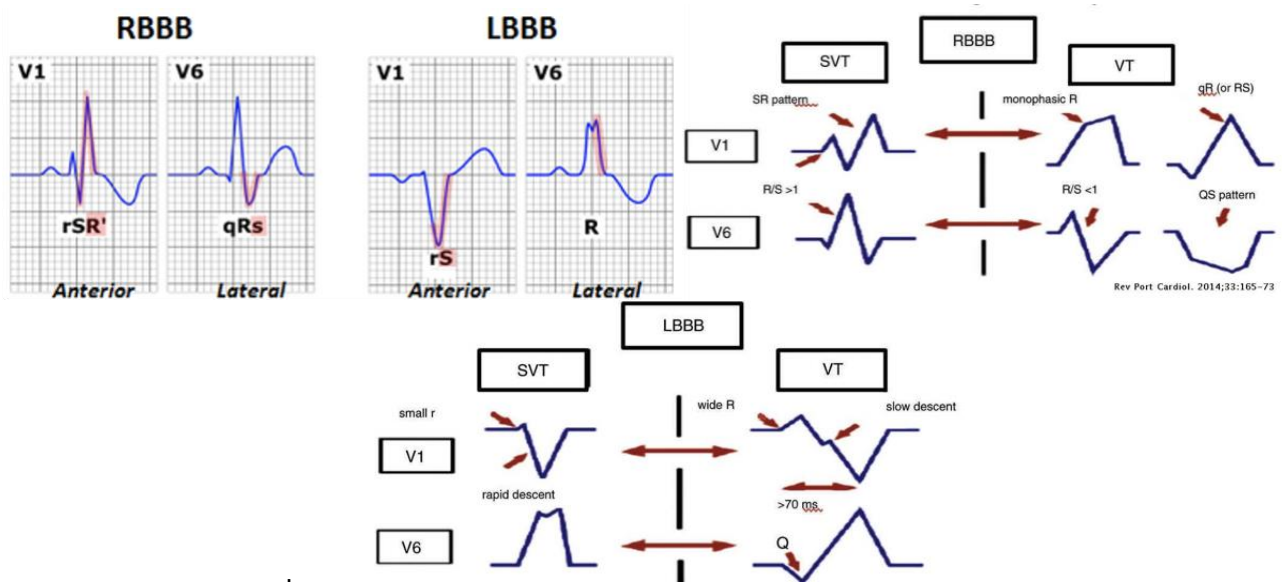
1. Consider the substrate:
   a. History of CAD or cardiomyopathy favors VT
   b. Young age, known history of atrial tachyarrhythmias, or baseline bundle branch block favors SVT with aberrancy
   c. Medications in overdose: Class 1A/3 antiarrhythmics, antipsychotics, antidepressants, antiemetics all favor WCT
2. Consider classical ECG features of VT:
   a. AV dissociation (including fusion/capture beats)
   b. Positive concordance (RS waves in V1-V6, suggesting basal VT focus)
   c. Negative concordance (QS waves in V1-V6, suggesting apical VT focus)
3. Consider the axis and the QRS width:
   a. Extreme axis deviation: northwest axis (positive in aVR, suggesting a ventricular focus or negative in I and AVF) or with a superior axis (II, III, aVF are negative)
   b. Wide QRS (RBBB > 140 ms, LBBB > 160 ms)
4. Consider using the Brugada Algorithm:

Brugada Algorithm



Clarifying the Brugada Algorithm:

1. Absence of an RS complex in all precordial leads? If yes, then VT.
    a. This basically means that the QRS morphology in every precordial lead is either a Q wave or an R wave - i.e. positive or negative concordance.
2. R to S interval >100 ms in one precordial lead? If yes, then VT.
    a. This criteria means that you find an RS complex in one of the precordial leads, and measure the distance from the beginning of the R wave to the nadir of the S wave. If this distance is > 100 ms, this is likely VT.
    b. Why? Well, in a typical RBBB or LBBB, remember that the other bundle is working normally. So the initial part of the RBBB or LBBB complex should be a quick (sharp deflection) because ventricular activation is occurring through the His-Purkinje system. The second part of the complex is wide/slurred, because electricity is moving through the myocardium (rather than through the conduction system, and thus is inherently slow) in order to depolarize the other ventricle.
    c. This means that if the initial part of QRS complex is wide (rS >100 ms), rather than a nice sharp deflection, that is more typical of direct myocardial activation (that is, VT), since typically conduction through the His-Purkinje tends to be much faster.
3. AV dissociation? If yes, then VT.
    a. AV dissociation, including fusion or capture beats (examples below), are consistent with VT.
4. Morphology criteria for VT present both in precordial leads V1-2 and V6.
    a. This criteria is more complicated, and comes down to an understanding of what a normal RBBB and LBBB should look like:

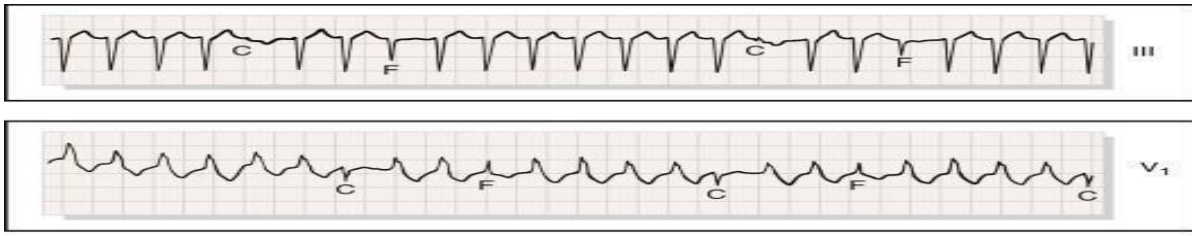


a. A typical RBBB looks like an RSR' complex in V1, with R smaller than R', and an RS complex in V6, with R/S >1. So any complex that looks significantly different than this (for example, a monophasic R, qR complex, or RSR' complex with R > R') favors a diagnosis of VT.
b. A typical LBBB looks like an rS complex in V1, and an R in V6. So any complex that looks significantly different than this (for example, a wide R wave or wide notched S wave in V1, or a Q wave in V6) favors a diagnosis of VT.

Additional Tips for Identifying Types of WCTs

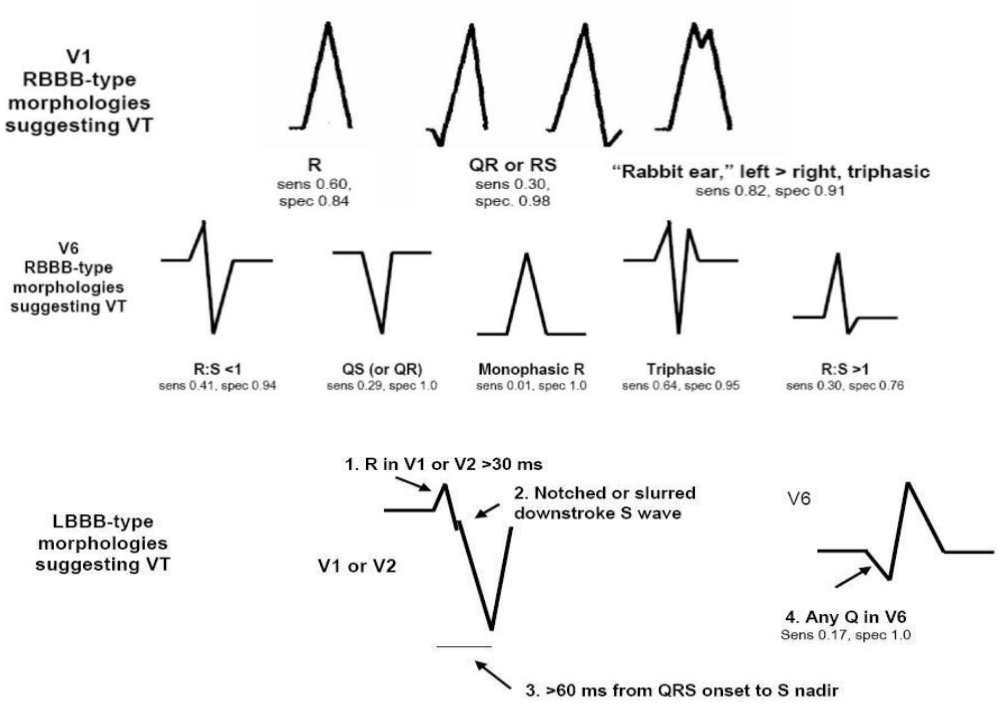
Examine the telemetry strip: Look for R-on-T at the start of the WCT, also look for AV dissociation (P waves marching through discordant to QRS, capture beats, fusion beats)

- Capture beat (labeled “C” in strip below): Atrial depolarization that is able to normally conduct a narrow QRS and transiently interrupts the spread of electricity from the VT focus
- Fusion beat (labeled “F” in strip below): Simultaneous conduction and blending on ECG of supraventricular beat and wide complex ventricular beat
- Beat-to-beat variability in QRS morphology: Characteristic in polymorphic VT or SVT/AF with varying degrees of pre-excitation/fusion or rate-related aberrancy.
- Pacer spikes: may indicate pacemaker etiology (paced QRS followed by retrograde P)



QRS morphology:

- A QRS > 160 msec has a 20:1 likelihood ratio of being VT. VT can be narrow (<140 msec) if it arises near the His-Purkinje system
- If LBBB or RBBB pattern, look for morphologies suggestive of VT:



Above V1 or V2 criteria, sens 1.0, spec 0.89

- Note: If there is VT with a RBBB pattern + inferiorly directed axis in a patient with a structurally normal heart, consider LVOT VT. Interestingly, this rhythm can respond to drugs that reduce cAMP, such as adenosine, verapamil or beta-blockers
- Note: If there is VT with a LBBB pattern + inferiorly directed axis in a patient with a structurally normal heart, consider **RVOT VT**. This rhythm also responds to drugs that reduce cAMP

There are many **formal criteria** for distinguishing VT from other causes of WCT with two others listed below in addition to the Brugada criteria discussed in depth above. They are more time consuming and unwieldy in comparison to the quick approach above. If in doubt, assume VT.

1. Vereckei criteria
2. R wave peak time (RWPT)

Clinical Management of WCT

Consider all WCT as VT until proven otherwise. At least 80% of WCT in patients with ischemic or structural heart disease is VT.

Initial Management According to Stability

- **Pulseless**: Immediately start the **pulseless VT ACLS algorithm** and prepare for unsynchronized DCCV
- **Hemodynamically unstable** or highly symptomatic: Prepare for synchronized DCCV (+ fentanyl/versed for sedation) and start amiodarone (150 mg x 1 Q 3–5 min, then drip @ 1 mg/min), and/or lidocaine (100 mg x 1, then drip @ 1–4 mg/min) unless concern for TdP (prolongs QTc)
  - Put pads on the patient
  - CALL FOR HELP:
    - Fellow resident(s) and your attending
    - Ward Cardiology fellow and/or EP Fellow on Call
    - RICU if anticipate potential need for intubation
    - Cardiac anesthesia for conscious sedation (though often no time)
  - Worry about etiology after stabilization
    - If regular, monomorphic, and there is some suspicion for SVT, consider adenosine as both a diagnostic (can slow down rhythm to make easier to dx) and therapeutic intervention
    - If pacemaker-mediated or tracked WCT→ **apply magnet**
- **Hemodynamically stable**:
  - Put pads on patient, call for help; you have *some* time to determine etiology of WCT, but *most patients do not tolerate persistent VT* (particularly if critically ill) and will likely develop hemodynamic instability

- If you suspect VT→ start **amiodarone and/or lidocaine**
- Be ready to cardiovert, consider cardioverting stable VT that persists for many minutes (requires the same algorithm as above)

Further Management According to Etiology

Monomorphic VT:

- Anti-arrhythmic drugs (AAD): Temporizing measure while reversing underlying cause. Do not reduce mortality or prevent SCD, may *increase* mortality when used as monotherapy for VT/VF prevention.
  - Recurrent, stable VT: Amiodarone and procainamide
  - WPW possible: Lidocaine or procainamide preferred (both reduce accessory pathway conduction)
    - **Amiodarone**: 150 mg IV bolus over 3–5 min (re-bolus as needed), *followed by gtt load at 1mg*/min for 6hrs and then 0.5 mg/min for 18 hours.
      - Effective for both ventricular and supraventricular arrhythmias (Na+ and K+ channel blocker; slows AV nodal conduction as well) and has superior efficacy over lidocaine
      - AV nodal blockade effects predominate until 6–7 grams administered. A full "amio load" for VT is 10 grams (given over a period of days)
      - AVOID IN TdP: nodal-blocking activity slows HR and K^+ channel blocking effect prolongs the QTc, which can promote TdP
    - **Lidocaine**: 1–1.5 mg/kg IV bolus over 2–3 minutes (often 100mg), *followed by* 1–4 mg/min infusion (often start at 1)
    - **Procainamide**: Infuse at 20–50 mg/min until arrhythmia is controlled (stop if hypotension or if QRS complex widens by 50% of original width, or total of 17 mg/kg is given). Maintenance infusion usually 1–6 mg/min
- Electrolytes: replete Magnesium and potassium
- Electricity: **Asynchronous DCCV** (for pulseless VT) vs **synchronized DCCV** (for VT w/ pulse). Other options if patient has a Pacemaker include:
  - Over-drive pacing (anti-tachycardia pacing) at a faster rate than the VT may be useful in some cases (call Ward fellow and/or EP for help w/ ATP).

Refractory monomorphic VT:

- Definitions: refractory to above pharmacologic measures
  - Incessant VT = Hemodynamically stable VT >1hr
  - VT Storm = Multiple bouts of unstable VT within 24hr
- Management:
  - Sedation with intubation: reduces autonomic tone
  - Treatment of underlying ischemia: revascularization, IABP support
  - Catheter-based ablation therapy: Radiofrequency (RF) ablation is often performed for refractory VT or VT storm. Acute procedural success (no inducible VT) rates are approximately 70%

Polymorphic VT:

- **Torsades/PMVT w/ prolonged QT** (on ECG from earlier in day)
  - Electrolytes: **Repletion of Mg^{2+} with 1–2 g IV bolus**, with a total dose of 2–4 g over 10–15 min, can successfully terminate TdP within 5 minutes in up to 75% of patients, and 15 minutes in most patients. Replete K^+ as well.
  - AAD: **Lidocaine** *avoid nodal agents and amiodarone*
  - Chronotropes: Goal **HR 80-100bpm will shorten the QTc** and can abort the PMVT. Start IV infusion of **isoproterenol** (2–6 mcg bolus *followed by* 2–20 mg/min OR **dopamine** at a starting rate of at least 300 mcg/min
  - Electricity: **Asynchronous DCCV** (for sustained PMVT) or **over-drive pacing** at rates in the range of 80–100 bpm (to suppress pause-dependent initiation of PMVT).
- **PMVT with normal QT** (on ECG from earlier in day) is **ischemia until proven otherwise** → ACS pathway with emergent cardiology evaluation for cath/revasc, can use AAD as above

SVT with Aberrancy:

- AAD: Treat as you would any other SVT; consider adenosine, BB, CCB, amiodarone, correct toxicities/drug effect/electrolyte abnormalities
- Electricity: Synchronized DCCV if unstable or refractory symptoms

SVT with Pre-Excitation:

- AADs
  - 1st line: **Procainamide** (1 gm over 50 min IV)
  - 2nd line: Ibutilide (0.01 mg/kg over 10 minutes, max dose 1 mg, can repeat once after 20 mins)
  - 3rd line: Amiodarone (150 mg IV x 1, can repeat many times→then 1mg/min gtt)

- Caution: Adenosine should not be used in pre-excited AF (presents as irregular, WCT); refer to AVRT section for management of SVT associated with WPW
- Electricity: DCCV for extremely symptomatic or unstable patients

Pacemaker-Mediated WCT:

- **Magnet** is 1st line therapy. Magnet will also stop the arrhythmia by mode switching to VOO or DOO to stop sensing the atria. The magnet does *not* change the pacing mode for an ICD (it will disable the defibrillator therapies) and thus will not terminate a PPM-mediated tachycardia in a patient with an ICD.
  - EP will need to reprogram pacemaker reprogramming to prevent further episodes of PMT
- AAD: 2nd line: Adenosine, verapamil or beta-blockers can abort retrograde conduction and stop the circuit

Pacemaker-Tracked WCT: Treat SVT as you would any other SVT. Mode switch PPM to a non-tracking mode either by EP interrogation or with magnet.

Maintenance Therapy

- **Devices**: ICDs are recommended for secondary prevention of VT/VF unless a reversible trigger is identified/treated
  - The AVID trial demonstrated a 10% absolute mortality benefit with this strategy when compared to AAD alone (see ICD Section for more information)
  - Specific guidelines are available for IHD, NICM, and other specific cardiomyopathies (e.g. HCM)
- **Medical management:**
  - Beta-blockers: reduce sympathetic tone, have some direct antiarrhythmic effect, and may reduce mortality in patients with previous VT/VF
  - AADs are often continued unless a reversible VT/VF trigger (e.g. ischemia) is identified and treated, although there is *no established mortality benefit* with this strategy
  - Patients with HFrEF should be treated with a BB, mineralocorticoid antagonist, ACEi/ARB/neprolysin inhibitor to reduce SCD and all-cause mortality
- **Procedures:**
  - Patients with VT/VF and ischemic heart disease should be revascularized as appropriate
  - VT ablation:
    - VT ablation is recommended in: patients with sustained VT that recurs despite AAD, when AAD are not tolerated, incessant VT without a reversible cause
    - Evidence:
      - Among the earliest trials in VT ablation was SMASH-VT (NEJM, 2007) in which VT ablation was associated with reduced incidence of ICD therapies.
      - The VANISH trial (NEJM, 2016) randomized patients to escalation of AAD versus VT in patients with ischemic cardiomyopathy with recurrent VT. VT ablation was associated with a 10% absolute reduction in the primary endpoint (composite of death, VT storm, ICD shocks); there was no difference in mortality
    - See *Chapter 5 – Electrophysiology Studies and Procedures for further details*

References:

1. Antunes, Eduardo, et al. "The differential diagnosis of a regular tachycardia with a wide QRS complex on the 12-lead ECG: ventricular tachycardia, supraventricular tachycardia with aberrant intraventricular conduction, and supraventricular tachycardia with anterograde conduction over an accessory pathway." *Pacing and clinical electrophysiology: PACE* 17.9 (1994): 1515
2. Trial, Cardiac Arrhythmia Suppre4ssion. "Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after acute myocardial infarction." *N. Engl. J. Med.* 321 (1989): 406-412
3. Jain, Rahul, et al. "Electrocardiographic features of arrhythmogenic right ventricular dysplasia." *Circulation* 120.6 (2009): 477
4. Bakker, Annelies LM, et al. "The Lewis lead: making recognition of P waves easy during wide QRS complex tachycardia." *Circulation* 119.24 (2009): e592-e593
5. Brugada, Pedro, et al. "A new approach to the differential diagnosis of a regular tachycardia with a wide QRS complex." *Circulation* 83.5 (1991): 1649-1659
6. Vereckei, András, et al. "New algorithm using only lead aVR for differential diagnosis of wide QRS complex tachycardia." *Heart rhythm* 5.1 (2008): 89-98
7. Exner, Derek V., et al. "Beta-blocker use and survival in patients with ventricular fibrillation or symptomatic ventricular tachycardia: the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial." *Journal of the American College of Cardiology* 34.2 (1999): 325-333
8. Defibrillators, Antiarrhythmics Versus Implantable. "Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias." *N Engl J Med* 337.22 (1997): 1576-1583
9. Sapp, John L., et al. "Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs." *New England Journal of Medicine* 375.2 (2016): 111-121
10. Tung, Roderick, et al. "Freedom from recurrent ventricular tachycardia after catheter ablation is associated with improved survival in patients with structural heart disease: an International VT Ablation Center Collaborative Group study." *Heart rhythm* 12.9 (2015): 1997-2007
11. Al-Khatib, Sana M., et al. "2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* 72.14 (2018): e91-e220

Conduction Diseases and Bradyarrhythmias

A narrow complex tachycardia (NCT) refers to a tachycardia with QRS duration <120ms and typically implies normal electromechanical conduction from a supraventricular origin. Generally, it is helpful to organize NCTs by mechanism (automaticity, re-entry, or triggered activity) and anatomic origin (sinus node, atria, AV node).

Management of Unstable Bradycardia: CALL CODE, *follow ACLS bradycardia protocol*

Protocol: **atropine** 0.5mg IV q3-5min (max 3mg) ? **transcutaneous pacing** +/- epinephrine gtt +/- dopamine gtt

Medications:
- **atropine** 0.5mg IV q3-5min (max 3mg) [*avoid in Mobitz II/CHB*]
- **dopamine** 5-15μg/kg/min (β_1 predominant; usually 200-800 μg/min)
- **epinephrine** 2-10μg/min
- **isoproterenol** 2-10μg/min
- **glucagon** 3-10mg bolus followed by 3-5mg/h gtt for βB or CCB overdose

Transcutaneous pacing
1. Place Zoll pads, sedate (ideally fentanyl/midazolam with Anesthesia present, but can use morphine/lorazepam if emergent)
2. set mode to pace, increase rate to 100bpm, and set pacing output (stimulus needed to capture) to 140mA (if code setting, otherwise start lower), and ensure capture w/ pulse.
3. Intubation is not necessary for pacing, but can be considered for airway protection as part of ACLS protocol
4. Will require placement of transvenous pacing wire *See Chapter 4 – Device Therapy*

Pathophysiology of Bradyarrhythmias

Broadly, bradyarrhythmias can be characterized by one of two mechanisms:
1. Failure of impulse generation: decreased or failed SA node automaticity can result in too few electrical impulses originating from the SA node. The most common bradyarrhythmia originating from the sinus node is *sinus bradycardia*. When symptoms develop from such slowed rates that symptoms develop, a patient is said to have *sick sinus syndrome*.
2. Failure of impulse propagation: when normal electrical impulses generated by the SA node (or another ectopic atrial pacemaker) are not conducted properly from the atria down to the ventricles (by way of the AV node and His-Purkinjie system) is termed *heart block*. This arises from abnormal conduction velocity and/or refractory periods throughout the conducting system, almost exclusively owing to disease of the AV node or His-Purkinjie conduction pathways.

Bradyarrhythmia by Site of Origin: SINUS NODE

Conduction disease involving the sinus node include sinus bradycardia and sinus node dysfunction

Sinus bradycardia

- ECG: HR less than 50-60 bpm, normal p wave axis
- Pathophysiology:
  - Most often *physiologic* and asymptomatic, seen in healthy individuals, endurance athletes, and during sleep where it is not uncommon to see rates briefly in the 30s or pauses of up to 2 seconds
  - *Pathophysiologic* causes include SA node dysfunction, medications, 15-25% of MI (RCA supplies SA node in 60% of individuals), sleep apnea, and exaggerated vagal tone (e.g. vasovagal syncope) (Circulation, 2020; 142:15)
- Treatment:
  - Acute, unstable: **Call code + initiate ACLS Bradycardia algorithm with immediate placement of temporary pacing pads on the patient (**see management of unstable bradycardia section)
  - Chronic treatment: See *Chapter 4 – Device Therapy* for indications for pacemaker therapy

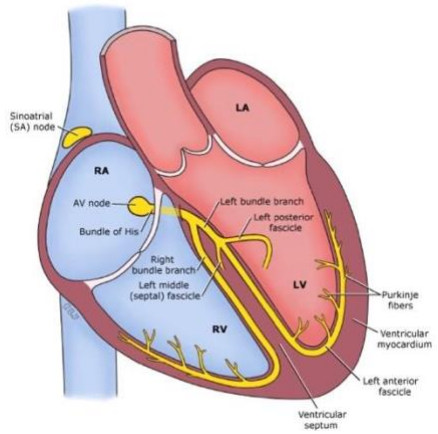
Sinus node dysfunction (SND) (formerly sick sinus syndrome)

- Presentation: symptomatic bradycardia (dizziness, palpitations, pre-syncope, syncope)
  - Numerous ECG abnormalities may contribute including Sinus bradycardia, Sinus pauses (greater or equal to 2 s), Sinus arrest, SA nodal exit block (delay in impulse leaving SA node), Chronotropic incompetence
  - If accompanied by SVT (atrial fibrillation, flutter, or tachycardia) can be termed *tachycardia-bradycardia syndrome*
- Pathophysiology: failure of SA node to generate HR that meets individual's physiologic needs
  - Most mechanism is SA node fibrosis, other causes include infiltrative disease (amyloid, sarcoid, hemochromatosis), inflammatory diseases (rheumatic fever, pericarditis, diphtheria, Chagas disease), SA nodal artery disease (most commonly RCA disease)
- Treatment
  - Acute, unstable: ACLS
    Chronic: medical therapy alone typically fails (due to unacceptable bradycardia with adequate control of tachycardia) often, a combination of meds (e.g., βB, CCB, digoxin) for tachycardia and permanent pacemaker for bradycardia

Bradyarrhythmia by Site of Origin: AV NODE and BELOW

Overview: Conduction diseases at the level of the AV node and Bundle of His typically refer to various *failures of impulse propagation*, or "AV blocks".

- When the block is within the AV node (first-degree or Mobitz I), subsidiary pacemakers at the AV junction usually take over the pacemaker function of the heart, resulting in a relatively stable, non-life-threatening heart rhythm.
- Infra-nodal blocks (within the His bundle) typically result in unstable escape rhythms that may require temporary or permanent pacing

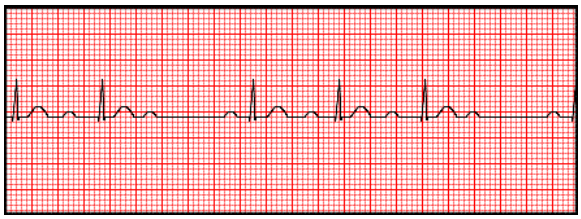


First degree AV block

- ECG**:** Prolonged PR (>200ms), all atrial impulses conducted (1:1)
- Pathophysiology: prolonged or slower conduction through the AV node
  - Monitoring prolongation of a PR interval may have clinical implications in patients in whom there is concern for aortic pathology, such as an aortic root abscess
- Treatment: Typically benign and asymptomatic with a narrow escape rhythm and with no indication for treatment.

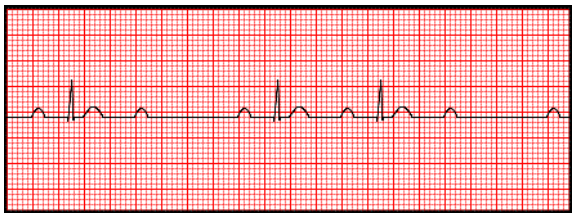
Second-Degree AV Block Mobitz Type I (Wenckebach)

- ECG: Progressive PR prolongation until an atrial impulse is not conducted
  - Look at the first PR interval after a pause; the PR after the pauses should be the shortest PR in Mobitz I
  - The relative increase in the PR interval decreases with each sequential beat; in other words, the PR intervals may look something like this: 220ms-->260ms-->280ms. This is why it is easiest to see a prolonging PR interval between the first and second beat of a cycle.
  - RR interval progressively shortens with each beat in the cycle prior to the dropped beat (due to the above phenomenon)
- Pathophysiology: reversible conduction delay within the AV node
  - *Physiologic*: high vagal tone such as athletes, young people
  - *Iatrogenic*: AV nodal blocking agents, post-cardiac surgery, post-ablation, post-TAVR
  - *Pathologic*: myocardial ischemia involving the conduction system (RCA usually supplies the AV node as well as SA node), cardiomyopathy, myocarditis (Lyme)
- Treatment: typically benign and asymptomatic, if symptomatic may warrant EP study to identify location of block (supra-His block i.e. AV node no treatment, infranodal may warrant PPM)



Second-Degree AV Block Mobitz Type II

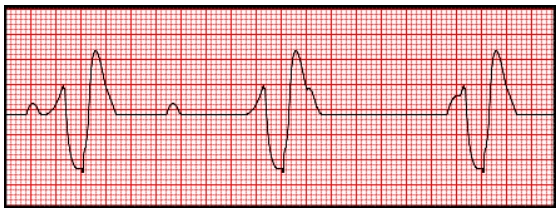
- ECG: intermittent non-conducted P-waves without progressive prolongation of the PR interval
  - Note: difficult to distinguish Mobitz type I vs II AV block on ECG if 2:1 block present (as there is no chance to observe PR prolongation)
- Pathophysiology:
  - Whereas a Mobitz I block suggests AV nodal disease, a Mobitz II block always indicates a more distal block below the AV node.
  - Etiologies overlap with Mobitz Type I (iatrogenic, pathologic), though *rarely seen in patients without underlying heart disease, often seen following anterior MI with infranodal conduction injury.*
- Treatment:
  - Mobitz Type II is an *unstable rhythm*, if identified, pacing pads should be placed and cardiology should be urgently involved for consideration of temp wire
  - Treat reversible causes if present (myocardial ischemia, electrolyte abnormalities, AV nodal agents, hypothyroidism)
    - If no reversible cause is identified, high likelihood of progression to complete heart block, therefore require PPM implantation during that admission *See Chapter 4 – Device Therapy*)



Third-Degree AV Block (Complete Heart Block)

- ECG: complete dissociation of atrial and ventricular conduction
  - Nearly all patients with complete heart block present with some degree of symptoms (fatigue, dyspnea, chest pain, pre-syncope, syncope, arrest) secondary to the typically slow (~ 40 bpm) escape rhythms
- Pathophysiology: Etiologies are similar to first- and second-degree AV block
  - Hemodynamics become entirely dependent upon subsidiary escape pacemaker which are typically fascicular or ventricular and therefore considered unstable

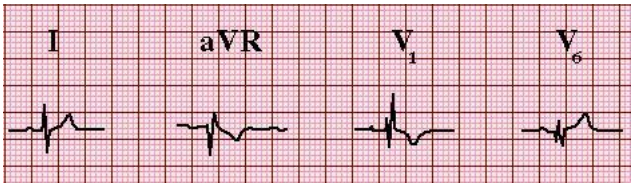
Treatment: Prepare for transcutaneous pacing while awaiting urgent temp wire placement and likely PPD implantation if no reversible cause can be identified and treated (*See Chapter 4)*



Bradyarrhythmia by Site of Origin: DISTAL (bundle and fascicular) BLOCKS

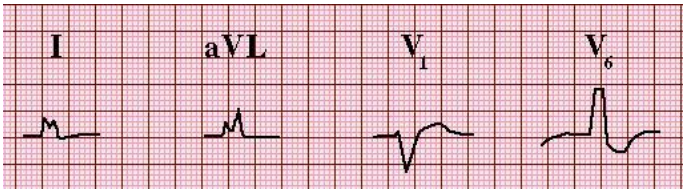
Right bundle branch block (RBBB)

- ECG criteria:
  - QRS > 120 ms ("*incomplete"* if less than 120 ms)
  - Rsr', rsR', rSR' in leads V1 or V2
  - S wave of greater duration than R wave or >40 ms in I and V6 in adults
  - Normal R peak time in leads V5 and V6 but > 50 ms in V1
  - Rightward axis; if left axis, then diagnostic of a bifascicular block (RBBB + LAFB)
- Pathophysiology: impaired conduction down the right bundle branch (see diagram above)
- Etiology: Most often idiopathic or associated with structural heart disease
  - Chronically increased RV pressures
  - Sudden increase in RV pressure stretch (e.g. PE)
  - Myocardial ischemia, infarct, or inflammation (e.g. myocarditis)
  - Cardiomyopathies, including congenital heart disease
  - Transient RBBB may be induced during right heart catheterization
- Treatment: none
- Prognosis: RBBB in setting of acute MI or CHF is associated with higher mortality **REFERENCE**



Left bundle branch block (LBBB)

- ECG
  - QRS > 120 ms ("*incomplete"* if less than 120 ms)
  - Broad notched R waves in I, aVL, V5, V6 with absent q waves in I, V5, V6
  - R peak time >60 ms in V5 and V6 but normal in V1, V2, V3
  - ST and T waves are in opposite direction of QRS ("*negative concordance*")
    - See ACS section: STEMI Sgarbossa criteria for discussion of ECG ischemia interpretation in setting of LBBB
- Pathophysiology: usually result of progressive degenerative disease of conduction system that can be hastened by common CV risk factors like HTN, CAD, DM
  - Other notable etiologies: ischemia (acute anterior MI), iatrogenic (septal myomectomy, TAVR)
- Treatment: see *Chapter 4 – Device Therapy* for indications (HFrEF, syncope)
- Prognosis: is an independent predictor of worse outcomes in CAD, MI, and CHF
  - MI: complicates diagnosis of MI (Sgarbossa interpretation), and may correlate with infarct size
  - CHF: LBBB produces disordered LV contraction which can further worsen systolic function



Chronic bifascicular blocks

- ECG: RBBB + left anterior fascicular block OR left posterior fascicular block
  - Left anterior fascicular block (LAFB): Left axis, QRS <120, qR in I, aVL, rS in II, III, aVF
  - Left posterior fascicular block (LPFB): Right axis, QRS <120, rS in I, aVL, qR in II, III, aVF
- Treatment: benign finding, though may warrant additional monitoring if history of syncope as intermittent LBBB + bifascicular block results in intermittent complete heart block that may require PPM

References:

Fogoros, Richard N. Electrophysiologic Testing. Chichester: Wiley-Blackwell, 2012.
Patterson E, Scherlag BJ et al. Decremental conduction in the posterior and anterior AV nodal inputs. Journal of Interventional Cardiac Electrophysiology (2002) 7 (2): 137–48.
Tisdale *et al.* Drug- Induced Arrythmias: A Scientific Statement From the American Heart Association. Circulation 142 (2020

Device Therapy

The purpose of this section is to review the specific indications for temporary pacing; permanent pacemakers (PPMs), cardiac resynchronization therapy (CRT), and implantable cardioverter-defibrillator (ICD) therapy.

Temporary Pacing

Transcutaneous Pacing

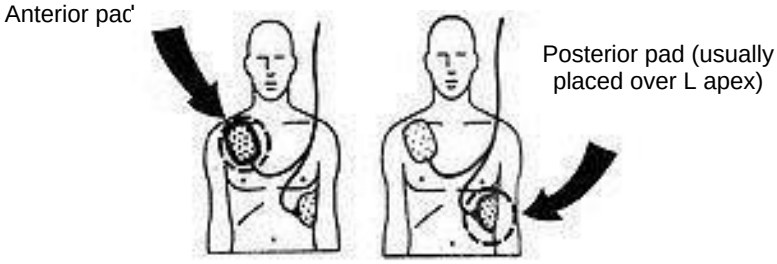
Indications: Formal indications for transcutaneous pacing are provided in Table 1 below. Indications for pad placement (to allow for transcutaneous pacing instantly if needed) are also included and designated by an asterisk. These patients will generally proceed to urgent insertion of transvenous pacing wire.

Table 1: Indications for Transcutaneous Pacing and Placement of Pacing Pads

Class I
Sinus bradycardia (HR <50) with symptomatic hypotension (SBP < 80), refractory to drug therapy† 3ºAVB† Mobitz Type II 2ºAVB† Bilateral BBB (alternating BBB or RBBB + alternating LAFB/LPFB)* Newly acquired or age LBBB, LBBB and LAFB, RBBB and LPFB* RBBB or LBBB and 1ºAVB*
Class IIa
Stable bradycardia (SBP >90, no hemodynamic compromise or responsive to pharmacologic therapy)* Newly acquired or age-indeterminate 1ºAVB*
Class IIb
Uncomplicated acute MI without evidence of conduction system disease*

† Indication for demand pacing, * Indication for pad placement only

1. **Place pads**: Note that all MGH defibrillators can provide transcutaneous pacing. Proper pad placement is shown in the figure below. Ensure that the pads are connected to the defibrillator and that the ECG leads are connected to the patient (white is right, smoke over fire = white lead on R shoulder, black lead on left shoulder, red lead on left leg) and the defibrillator.



2. **Administer sedation**: Involve anesthesia for all non-ACLS protocol transcutaneous pacing to assist with administration of medications that may cause respiratory compromise (such as IV midazolam/fentanyl). If pacing must be initiated immediately, IV Dilaudid +/- IV Ativan may be used.
3. **Initiate Pacing**: Turn the defibrillator dial to “pacer” and set the pacing rate and output, which is the electrical stimulus needed to produce capture; a higher output represents more energy and will generally be more painful. A reasonable initial rate and output are 100 bpm and 100 mA, but note that the upper limit is around 140 mA. In non-emergent situations where you do not need to ensure immediate capture, it is reasonable to start with a lower output around 40 mA and increase by 5-10 mA until capture is achieved.
4. **Verify Capture**: Because the pacing rate should be well above the patients native rate, all beats should be paced. Appropriate capture is confirmed if pacing spikes precede all QRS complexes (and fire at the set rate, e.g. 100 bpm). If this is not the case, increase the output by 5-10 mA up to 140 mA. Confirm that paced/captured beats are perfusing with either palpation or Doppler of femoral pulse.
5. **Set Final Output**: If capture is achieved immediately (e.g. with an initial output set to 100 mA), find the capture threshold by decreasing the output slowly until capture is lost. The minimum output needed to maintain output will then be 10% higher than the capture threshold. In healthy patients, theoretical thresholds should range from 40-80 mA (corresponding to an output range of 44-88 mA or, more practically, 45-90). In clinical practice, thresholds tend to be more variable, with a range between 20-140 mA.

Transvenous Pacing

Indications: Transvenous pacing is a more durable option than transcutaneous pacing and is employed as a temporary bridge to recovery or to PPM placement.

Table 2: Indications for Transvenous Pacing

Class I
● Asystole ● Symptomatic bradycardia ● Bilateral BBB (alternating BBB or RBBB w/ alternating LAFB/LPFB) ● New or age-indeterminant bifascicular block (RBBB w/ LAFB/LPFB + first degree AVB) ● Mobitz Type II second degree AVB
Class IIa
● RBBB with 1ºAVB ● New or age-indeterminate LBBB ● Incessant VT for overdrive pacing ● Recurrent sinus pauses (> 3 sec) not responsive to atropine
Class IIb
● Age-indeterminate bifascicular block ● New or age-indeterminate RBBB
Non-guideline based but commonly encountered indications
● AVB after MI or cardiac surgery ● AVB due to Lyme disease or infective endocarditis (e.g. aortic paravalvular abscess) ● Intra/post-procedural support for AVNRT ablation, alcohol septal ablation, heart transplant, or TAVR ● Overdrive pacing for polymorphic VT

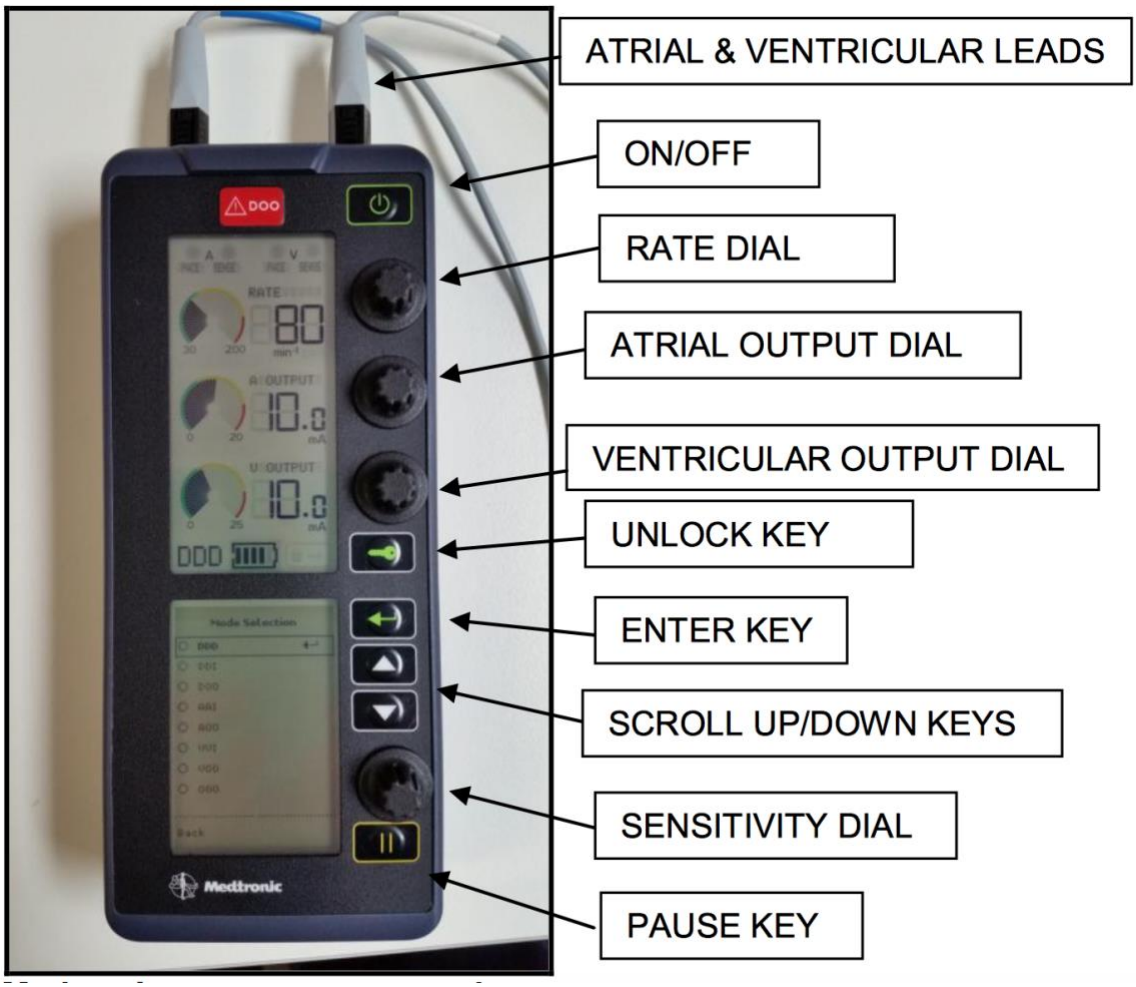
Special considerations: In contrast to transcutaneous pacing (which can be performed urgently without input from cardiology), placement of a temp wire for transvenous pacing must be performed in the cath lab. The pacing lead is inserted into the right ventricle via the right internal jugular, left subclavian, or femoral veins (less reliable and increased risk for dislodgement). Temp wires may remain in place for up to 7-10 days but carry a risk of infection. For this reason, prophylactic antibiotics are indicated during and after implantation.

Additional **complications** include: lead dislodgement, bleeding, RV perforation, tamponade, thrombophlebitis, PE or air embolism, pneumothorax, subdiaphragmatic stimulation, arrhythmias (ectopy/asystole), and/or permanent RBBB.

Temporary Pacing Settings:

The control box has four set parameters (Figure 1):

- **Heart Rate**: This sets the backup/pacing rate (if rate set to 80, pacing will only occur if intrinsic rate is < 80)
- **Output**: Electrical stimulus (mA) needed to produce capture (often set 5-10x higher) to ensure reliable capture. Must be assessed daily, as increased threshold may be an early sign of lead malfunction (e.g. migration, fracture). Note that the control box has separate dials for the atrial lead (if present) and ventricular lead (always present). Most medical patients will have only a single RV lead. In contrast, post-cardiac surgery patients with epicardial wires will often have both atrial and right ventricular leads.
- **Pacing Mode**: Most often set to VVI (ventricular pacing and sensing, allowing for inhibition of pacing if native rate is sensed at or above the backup rate)
- **Sensitivity**: Sets the device detection limit and represents the minimum energy generated by the heart that the device can detect. If the sensitivity is too low, the device will fail to detect intrinsic cardiac activity and may fire inappropriately. Alternatively, if the sensitivity is too high, the device may fail to fire



To test the output threshold:

1. Increase heart rate on device such that all beats are paced
2. Decrease output until pacing ceases and native rhythm is seen, this defines the output threshold of the temporary pacer
3. Increase output back up to its initial value (or 5-10x the threshold) and turn the rate back to its initial value
4. Do not touch sensitivity, unless troubleshooting
5. Document the threshold, output (in mA), and patient's native (underlying) rhythm

Note that for RV pacing, the ECG should show LBBB, with left superior axis-usually upright in I and aVL. Any change in pacing morphology is lead displacement until proven otherwise. If there is concern for change in lead position, perform threshold testing again and get a STAT CXR.

Troubleshooting common issues:

Failure to pace: Absence of pacing spikes and no paced QRS:

1. **Oversensing**: pacer senses noise artifact (background activity) as a QRS complex and does not pace. Decrease sensitivity or turn off sensing (asynchronous pacing, VOO).
2. **Battery or connection problem**: Replace battery and check connections.

Failure to capture: pacing spikes present but no paced QRS complex.

1. **Increased capture threshold due to fibrosis**. Increase output to capture.

2. **Lead migration** (epicardial lead migration can result in ventricular perforation). Troubleshoot with unipolar ECG: connect V1 electrode to distal-most pacing electrode. Normal endocardial contact should result in negative QRS deflection with ST elevation. A positive or biphasic QRS is suggestive of lead migration.
3. **Physiologic effect**: Such as ischemia, hypoxia, acidosis, alkalosis, hyperglycemia, hypercapnia, medication related. Attempt to reverse the underlying condition
4. **Battery or connection problem**. Replace battery and check connections.

Failure to sense: The device does not detect intrinsic cardiac activity and fires inappropriately. Pacing spikes can be seen on top of or after native QRS (increases risk of R on T).

1. **Lead migration**. Troubleshoot as above.
2. **Sensitivity too low**. Troubleshoot by increasing the sensitivity on the control box.
3. **Ectopic beats**. Consider/address reversible causes such as electrolytes
4. **Pulse generator failure**. Troubleshoot by replacing generator

Permanent Pacing

Permanent pacing is indicated for symptomatic or dangerous forms of bradycardia that are not due to transient or reversible causes.

Table 3: Class I Indications for Implantable Pacemaker

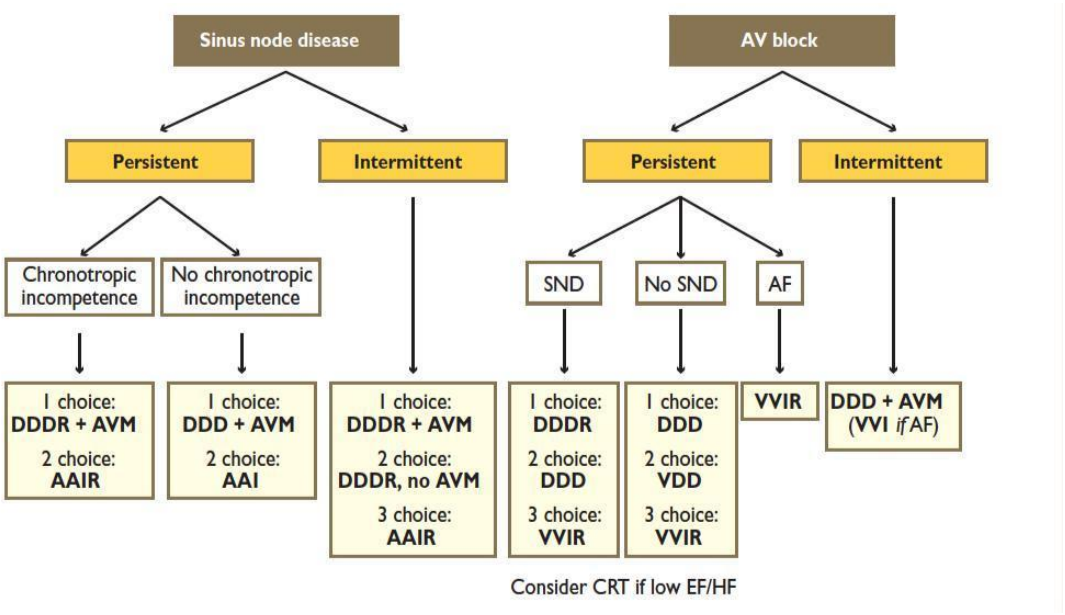
Sinus Node Dysfunction
Symptomatic bradycardia or frequent, symptomatic sinus pauses Symptomatic chronotropic incompetence Symptomatic bradycardia resulting from drug therapy or medical conditions
AVB
○ 2°AVB causing symptomatic bradycardia ○ 2° or 3°AVB during exercise without evidence of myocardial ischemia ○ 3°AVB with HR≥40 if cardiomegaly or LV dysfunction present or if block below AV node ○ 3° or adv. 2°AVB causing symptomatic bradycardia or VT/VF ○ 3° or adv. 2°AVB and awake/asymptomatic in NSR w/ pause ≥3s, infranodal escape or escape HR<40 ○ 3° or adv. 2°AVB and awake/asymptomatic in AF w/ bradycardia and pause ≥5s ○ Persistent 3° or advanced 2°AVB occurring after AV node ablation or cardiac surgery
Chronic Bifascicular Block
Advanced 2° or 3°AVB Type 2° with alternating bundle branch block
AV Block after Acute MI
Persistent and symptomatic 2° or 3°AVB Persistent 2° infranodal AVB with alternating BBB or 3° infranodal AVB
Hypersensitive Carotid Sinus Syndrome/Neurocardiogenic Syncope
Recurrent syncope due to spontaneous carotid sinus stimulation with asystole ≥3 seconds

Pacemaker modes:

There are many different pacing modes which are designated by a 1-5 letter code, although typically only the first three positions are used in practice.

NASPE/BPEG Codes for Pacing Operating Modes			
Position I	**Position II**	**Position III**	**Position IV**
Chamber(s) Paced	Chamber(s) Sensed	Response to Sensing	Rate Modulation
O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T =Triggered	R = Rate Modulation
V = Ventricle	V = Ventricle	I = Inhibited	
D = Dual (A+V)	D = Dual (A+V)	D = Dual (A+V)	

Figure 4: Algorithm for Choice of Optimal Pacing Mode



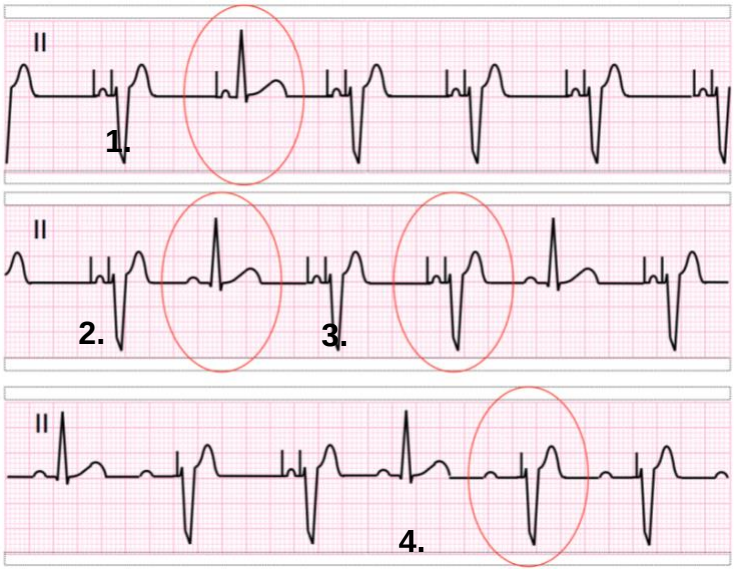
Note: AVM: AV delay management, SND: Sinus node dysfunction, AF: Atrial fibrillation, CRT: Cardiac resynchronization therapy.

AAI: Single right atrial lead paces unless native atrial activity is sensed. Useful for patients with isolated sinus node dysfunction, manifesting as sinus bradycardia or sinus pauses. Rate-responsiveness can be added for patients who cannot accelerate their heart rates (AAI-R). Patients must have intact AV conduction. A major disadvantage is that there is no protection from ventricular bradyarrhythmias in the setting of AV block which develops in 0.6–5% of patients with sick-sinus syndrome per year. Pacemaker upgrade is often a higher-risk procedure than *de novo* implantation of a dual-chamber system. In patients with sinus node dysfunction, the presence of bundle-branch block at implantation is a relatively accurate predictor of subsequent AV block, and dual chamber pacemaker should be considered instead.

VVI: Single right ventricular lead with paces unless ventricular activity is sensed. Very common mode for prevention of ventricular bradyarrhythmias or asystole. Virtually all devices currently in use are capable of VVI(R) pacing. Unlike AAI pacing, VVI pacing is effective even in patients with impaired AV conduction or in patients at risk for future development of AV block. VVI(R) pacing in particular is indicated in patients with chronic atrial fibrillation with a slow ventricular response. The drawback to VVI pacing is that this mode cannot maintain AV synchrony and lack of AV synchrony can result in pacemaker syndrome as well as increased risk of atrial fibrillation.

DDD: Right atrial and right ventricular leads which are both capable of pacing in the absence of native activity sensed in either respective chamber, but inhibited if it is. Provides closest mimic of physiologic pacing conditions and maintains AV synchrony which reduces the risk of AF in sick sinus syndrome, resulting in a lower incidence of thromboembolic events, improves hemodynamics by preserving the atrial kick, and helps to avoid pacemaker syndrome. Results in one (or more at any given time) of four different rhythms: normal sinus rhythm, atrial pacing with intact AV conduction, AV sequential pacing, and atrial sensing and ventricular pacing (P-synchronous ventricular pacing).

Figure 5: The “Four Faces” of DDD pacing



1: a-paced, v-sensed. 2: a-sensed, v-sensed (normal conduction). 3: a-paced, v-paced. 4: a-sensed, v-paced.

Subsection References:

1. Tracy, Cynthia M., et al. "2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* 61.3 (2013): e6-e75
2. Kusumoto, Fred M., et al. "2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* (2018): 25701
3. Trohman, Richard G., Michael H. Kim, and Sergio L. Pinski. "Cardiac pacing: the state of the art." *The Lancet* 364.9446 (2004): 1701-1719
4. Fitzpatrick, Adam, and Richard Sutton. "A guide to temporary pacing." *BMJ: British Medical Journal* 304.6823 (1992): 365
5. Gammage, Michael D. "Temporary cardiac pacing." *Heart* 83.6 (2000): 715-720

Implantable Cardioverter-Defibrillator (ICD) Therapy

Overview**:** These devices have been shown to be 97% effective in terminating arrhythmias with defibrillation, cardioversion or antitachycardia pacing (ATP). Additionally, **all ICDs can function as a pacemaker** (though note that the reverse is not true). ICDs can be **single-chamber (RV-lead) or dual chamber (RA/RV-lead) devices.** They can be distinguished from dual chamber PPMs on CXR by presence of coils.

Indications**:** Per AHA/ACC guidelines,[1-3] implantation of ICD should be considered in patients on optimal medical therapy who have an estimated survival of at least 1 year (with good functional status). There are Class I indications for both primary and secondary prevention, as well as Class II indications for conditions that increase the risk of SCD.

Class I
Secondary Prevention: Survivors of cardiac arrest due to VF or sustained VT without reversible causes

Primary Prevention:

- Ischemic cardiomyopathy and LVEF ≤ 30-40% at least 40 days post-MI (DINAMIT) or at least 3 months post-CABG (CABG-PATCH)
- LVEF ≤ 30% and NYHA Class I, II, or III (MADIT-II)
- LVEF ≤ 35% and NYHA Class II or III (SCD-HeFT)
- LVEF ≤ 40% and inducible VF or sustained VT at EP study (MUSTT)
- Non-ischemic cardiomyopathy with at least 3 months of documented
- CHF, LVEF ≤ 35%, and NYHA Class II or III (SCD-HeFT)*
- Syncope of unknown origin and VT/VF induced at EP study
- Spontaneous sustained VT (+/- hemodynamic instability) with structural heart disease (*DANISH Study: RCT of non-ischemic heart failure with EF ≤ 35%, showed no overall mortality benefit from ICD versus optimal medical therapy, however risk of SCD was reduced and a mortality benefit was observed in the subgroup that was <68 years old)

Class II
For numerous conditions that increase risk of SCD, with limited RCT data

- Hypertrophic cardiomyopathy: LV thickness >/= 30mm, family history of SCD, abnormal exercise BP
- Arrhythmogenic right ventricular cardiomyopathy (ARVC): extensive RV, LV involvement
- Long-QT syndrome: syncope and/or VT while on beta-blockers
- Brugada syndrome: syncope and/or VT
- Catecholaminergic polymorphic VT: syncope and/or sustained VT on beta-blockers
- Cardiac sarcoid, giant cell myocarditis, Chagas disease
- Unexplained syncope, significant LV dysfunction, and non-ischemic dilated cardiomyopathy
- Sustained VT with normal ventricular function
- Non-hospitalized patient awaiting heart transplant

Cardiac Resynchronization Therapy (CRT)

CRT is an important therapy among patients with HFrEF which portends a robust mortality and reverse remodeling benefit. Initially shown to improve exercise capacity, clinical symptoms, and LVEF in the MIRACLE Study. Further investigation demonstrated a mortality benefit in patients with HFrEF and widened QRS.

CRT implantation involves RA, RV, and coronary sinus (for epicardial pacing of LV) leads. This allows for optimization of A-V synchrony as well as V-V synchrony, which has been shown to improve stroke volume. For this reason, CRTs represents an important component of guideline directed medical and device therapy. CRT devices may only provide BiV pacing (CRT-P) or may allow for BiV pacing plus defibrillation with ICD function (CRT-D).

Indications for CRT are divided into two groups, those in sinus rhythm (table 4) and those who are in persistent or permanent atrial fibrillation who either cannot undergo ablation or who have received ablation and failed (table 5). For those who fall into those mentioned groups with atrial fibrillation, further consideration can be for AV junction ablation and simultaneous CRT which can both improve symptoms and reduce mortality (see figure 5 for further decision making and patient selection for ablation and/or CRT) in patients who either cannot tolerate or who do not respond to other methods of rate and rhythm control with the understanding that AVJ ablation will effectively render them pacemaker dependent. Most of the evidence for either group of patients are based on RCT's who enrolled patients who are NYHA II-IV with LVEF 35% or less with some exceptions in the atrial fibrillation groups detailed below who have received optimal medical therapy or OMT for at least 3 months after being diagnosed with HFrEF or at least 40 days following diagnosis of a myocardial infarction in addition to treatment of any reversible cardiomyopathy such as ischemic or tachycardia-induced cardiomyopathy. Additional recommendations for those with pre-existing ICD's can be found in the 2021 ESC guidelines on cardiac pacing and cardiac resynchronization therapy from which the below tables are pulled.[15]

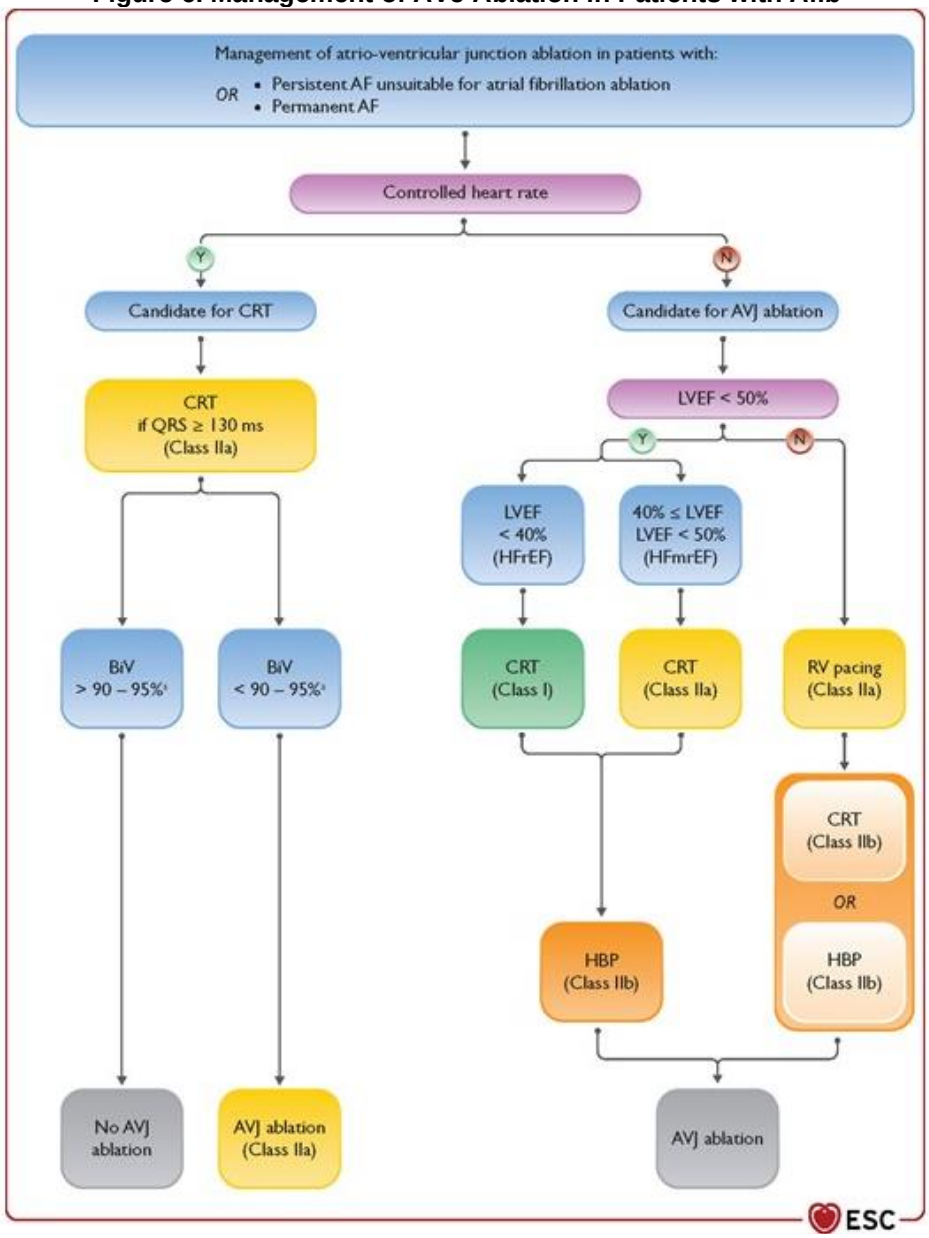
Table 4: 2021 ESC/EHRA Guidelines for CRT for patients in SR

Recommendations	Class[a]	Level[b]
LBBB QRS morphology		
CRT is recommended for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.[37,39,40,254–266,283,284]	I	A
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.[37,39,40,254–266,283,284]	IIa	B
Non-LBBB QRS morphology		
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.[37,39,40,254–266,283,284]	IIa	B
CRT may be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.[273–278,281]	IIb	B
QRS duration		
CRT is not indicated in patients with HF and QRS duration <130 ms without an indication for RV pacing.[264,282]	III	A

Table 5: 2021 ESC/EHRA Guidelines for CRT for patients in Afib

Recommendations	Class[a]	Level[b]
1) In patients with HF with permanent AF who are candidates for CRT:		
1A) CRT should be considered for patients with HF and LVEF ≤35% in NYHA class III or IV despite OMT if they are in AF and have intrinsic QRS ≥130 ms, provided a strategy to ensure biventricular capture is in place, in order to improve symptoms and reduce morbidity and mortality.[302,306,307,322]	IIa	C
1B) AVJ ablation should be added in the case of incomplete biventricular pacing (<90–95%) due to conducted AF.[297–302]	IIa	B
2) In patients with symptomatic AF and an uncontrolled heart rate who are candidates for AVJ ablation (irrespective of QRS duration):		
2A) CRT is recommended in patients with HFrEF.[196,197,306,308]	I	B
2B) CRT rather than standard RV pacing should be considered in patients with HFmrEF.	IIa	C
2C) RV pacing should be considered in patients with HFpEF.[188,196,323]	IIa	B
2D) CRT may be considered in patients with HFpEF.	IIb	C

Figure 6. Management of AVJ Ablation in Patients with Afib



References:

1. Tracy, Cynthia M., et al. "2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* 61.3 (2013): e6-e75
2. Kusumoto, Fred M., et al. "2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* (2018): 25701
3. Higgins, Steven L. "Impact of the Multicenter Automatic Defibrillator Implantation Trial on implantable cardioverter defibrillator indication trends." *The American journal of cardiology* 83.5 (1999): 79-82
4. Klein, Helmut U., and Sven Reek. "The MUSTT study: evaluating testing and treatment." *Journal of Interventional Cardiac Electrophysiology* 4.1 (2000): 45-50
5. Moss, Arthur J., et al. "Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction." *New England Journal of Medicine* 346.12 (2002): 877-883
6. Bardy, Gust H., et al. "Amiodarone or an implantable cardioverter–defibrillator for congestive heart failure." *New England Journal of Medicine* 352.3 (2005): 225-237
7. Hohnloser, Stefan H., et al. "Prophylactic use of an implantable cardioverter–defibrillator after acute myocardial infarction." *New England Journal of Medicine* 351.24 (2004): 2481-2488
8. Myerburg, Robert J. "Implantable cardioverter–defibrillators after myocardial infarction." *New England Journal of Medicine*359.21 (2008): 2245-2253
9. Tang, Anthony SL, et al. "Cardiac-resynchronization therapy for mild-to-moderate heart failure." *New England Journal of Medicine* 363.25 (2010): 2385-2395
10. Bristow, Michael R., et al. "Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure." *New England Journal of Medicine* 350.21 (2004): 2140-2150
11. Cleland, John GF, et al. "The effect of cardiac resynchronization on morbidity and mortality in heart failure." *New England Journal of Medicine* 352.15 (2005): 1539-1549
12. Curtis, Anne B., et al. "Biventricular pacing for atrioventricular block and systolic dysfunction." *New England Journal of Medicine* 368.17 (2013): 1585-1593
13. Ruschitzka, Frank, et al. "Cardiac-resynchronization therapy in heart failure with a narrow QRS complex." *New England Journal of Medicine* 369.15 (2013): 1395-1405
14. Olgin, Jeffrey E., et al. "Wearable cardioverter–defibrillator after myocardial infarction." *New England Journal of Medicine*379.13 (2018): 1205-1215.
15. Michael Glikson et al, ESC Scientific Document Group, 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: Developed by the Task Force on cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology (ESC) With the special contribution of the European Heart Rhythm Association (EHRA), *European Heart Journal*, Volume 42, Issue 35, 14 September 2021, Pages 3427–3520.
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Electrophysiology Studies and Procedures

The purpose of this section is to provide background/basic information on three commonly employed EP procedures: synchronized cardioversion and defibrillation, diagnostic EP studies, and catheter ablations.

Synchronized Cardioversion and Defibrillation

Cardioversion (DCCV) and defibrillation are non-invasive interventions that can terminate tachyarrhythmias by delivering an electrical shock to the heart. Cardioversion is performed by synchronizing the shock to a QRS complex while defibrillation is unsynchronized and delivers a random shock during the cardiac cycle.

Indications and Contraindications

Emergent DCCV and defibrillation are indicated in cases of clinical instability. Elective DCCV may also be performed as an effective treatment for SVTs.

Table 1: Cardioversion & defibrillation indications and energy dosing

CARDIOVERSION	**Monophasic (J)**	**Biphasic (J)***
AVRT/AVNRT[1]	50-100	<50-100
Atrial flutter[2]	100	50-100
Atrial fibrillation[2]	200	120-200
VT (with pulse)	200	100
DEFIBRILLATION		
VT (pulseless)	360	150-200
VF	360	150-200

[1]includes reentry arrhythmias AVRT and AVNRT (attempt adenosine first)
[2]includes:

AF/AFL of ≥48h (or unknown) duration and anticoagulated for 3–4 weeks (INR 2–3)

AF/AFL of <48h duration, for which anticoagulation is optional depending on risk
AF/AFL of unknown duration with CHF and absence of thrombus in LA on TEE acute onset AF/AFL with hemodynamic compromise: MI, pulmonary edema, hypotension
*All MGH defibrillators are biphasic which are typically effective at lower energy levels. Large patients may be difficult to cardiovert/defibrillate even at 360 J biphasic.

In general, **DCCV/defibrillation is contraindicated in the following cases**:

1. Known atrial or ventricular thrombus without emergent indication
2. Unknown duration AF/AFL without anticoagulation (unless with TEE or emergent)
3. Rhythms associated with increased automaticity or triggered activity (MAT, junctional tachycardia, AIVR) which typically recur within seconds after shock, and the release of endogenous catecholamines from the shock may further exacerbate the arrhythmia.
4. Digitalis toxicity
5. Severe electrolyte imbalance

Additionally, the following considerations exist for these **special populations**:

1**. Patients who are pregnant**: Can be performed without affecting the rhythm of the fetus. Fetal heart rate monitoring during the procedure is recommended.

2. **Patients who have pacemakers/ICDs**: Can be performed but the electrode should be > 12 cm from the pulse generator and an anteroposterior electrode orientation is recommended. The pacemaker/ICD should be interrogated afterward to ensure proper functioning.

Mechanism and Procedure

The delivered shock depolarizes all or most excitable cardiac tissue and induces a refractory period that terminates reentrant activity. Cardioversion restores sinus rhythm in 70–95% of patients. Efficacy decreases with increased resistance (tissue density, physical distance due to habitus), prolonged arrhythmia duration, presence of structural heart disease, and involvement of multiple reentry circuits.

Step-by-step instructions for **emergent cardioversion and defibrillation:**

Cardioversion:

16. Turn the mode selector to DEFIB (red area). Select the desired energy using the up and down arrow keys in the front panel. See above for desired energy, or in general:
    a. Narrow, regular: 50 – 100 J (atrial flutter often converts with 50 J)
    b. Narrow, irregular: 120 – 200 J (atrial fibrillation typically requires 150 J)
    c. Wide, regular: 100 J
    d. Wide, irregular: 150 – 200 J (defibrillation dose)
17. Press the Sync On/Off button
    a. Confirm that a Sync marker appears on the monitor above each detected R wave to indicate where discharge will occur
    b. If necessary, use the LEAD and SIZE buttons to establish settings that yield the best display
18. Press the CHARGE button on the front panel
19. Ensure all are clear from the bed then press and hold the illuminated SHOCK button on the front panel. The defibrillator will discharge with the next detected R wave
20. If additional shocks are necessary, increase the energy level as needed

Defibrillation:

1. Turn the mode selector to DEFIB (red area)
    a. The unit displays DEFIB 120J SEL on the monitor
    b. The default energy selections for adult patients are Shock 1: 120J, Shock 2: 150J, Shock 3: 200J. You can use energy select (UP and DOWN arrow keys) to change settings
2. If the monitor shows a shockable rhythm, press the CHARGE button on the front panel. If patient is pulseless, continue CPR while charging
3. Ensure all are clear from the bed then press and hold the illuminated SHOCK button
4. If patient is pulseless, resume CPR for 2 minutes before the next pulse and rhythm check

For **non-emergent and routine procedures:** NPO for at least 6-8h. Some patients may require periprocedural anticoagulation to prevent thromboembolism. TEE is frequently used to look for the presence of a LA thrombus.

Complications: After shocking, ST & T wave changes may occur and typically resolve within 5 minutes. However, the following complications may also occur:

- **Arrhythmias/Conduction abnormalities**:
  - Self-limited and include sinus tachycardia, PAC, PVC, NSVT, VT, VF, and LBBB.
  - May cause hemodynamic instability requiring further intervention
- **Thromboembolism**: Approximately 1% with anticoagulation, 5% without anticoagulation
- **Myocardial necrosis**: Severity depends on strength and number of shocks delivered
- **Myocardial dysfunction/stunning**:
  - Global LV dysfunction can be present until 48 hours after shock
  - Interpret cardiac studies within this 48h window with caution
- **Pulmonary edema**: Rare complication seen in patients with AF and/or LV dysfunction
- **Hypotension:** Transient, may last several hours, typically fluid-responsive
- **Cutaneous burns**:
  - Seen in 20-25% of patients
  - May use prophylactic steroid cream or topical NSAIDs at the site of electrodes

Electrophysiology Study (EPS)

EPS is an elective, invasive, intracardiac catheter-based intervention that measures specific intervals within the cardiac cycle to better understand the etiology, clinical significance, and management of brady- and tachy-arrhythmias.

Indications:

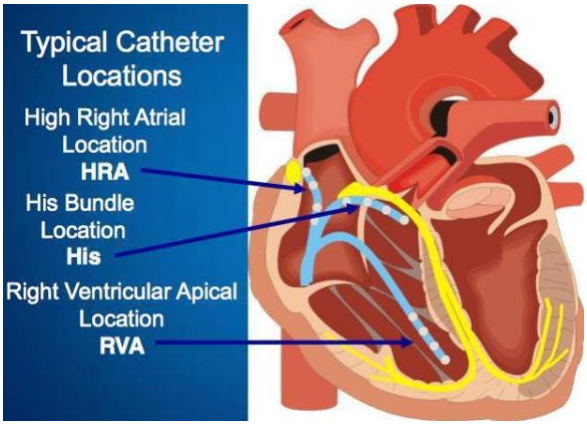
1. **Bradyarrhythmias**: acquire corroborative data in symptomatic patients with episodic bradyarrhythmia or define level of AV conduction abnormality
2. **Tachyarrhythmias**: define mechanism of NCT or WCT or reproduce a clinically defined tachycardia for mapping and ablation
3. **ICD implantation and programming**: search for EPS-induced VT or VF in patients with structural heart disease, NSVT, or reduced LVEF to justify ICD implantation and define optimal ICD parameters
4. **Syncope of unknown etiology**: to assess SN function, AV conduction, and search for VT/VF in patients with syncope and organic heart disease
5. **After cardiac surgery**: to assess the effect of cardiac surgery on arrhythmia risk

Contraindications: active ACS, bacteremia, ADHF (not caused by the arrhythmia), critical AS, severe HOCM, severe left main or 3-vessel CAD, presence of a major bleeding diathesis, presence of an acute lower extremity DVT (if femoral vein cannulation is required).

Mechanism and Procedure

Performed in the EP lab and patients are given at least conscious sedation. Standard ECG leads and defibrillation pads are applied. Multiple sites of venous (and at times, arterial) access are acquired for intracardiac catheter placement. Femoral access is most common. Catheters with electrode tips are placed in specific locations to both pace and record.

- High right atrium: Reflects SA node function, conduction, and direction of atrial activation
- Coronary sinus: Reflects LA activation. patients with SVT or pre-excitation
- Tricuspid annulus (His): Tracings from low His bundle, and high septal RV depolarization bundle activity
- RV apex: Reflects RV activity
- Left heart (via **transseptal or retrograde approach** for mapping/ablation)



AV

Obtained in

septal RA, reflect His

aortic

Mapping

At the conclusion of the diagnostic EPS, a subset of patients may undergo additional mapping and ablation for treatment of an arrhythmia. The created “map” is used to guide and localize potential ablation sites. Mapping prior to ablation is not necessary for certain types of arrhythmias that have a defined anatomical course (i.e. typical atrial flutter).

Catheter Ablation Therapy

Indications

1. WPW, accessory pathway-mediated, and other variant pre-excitation states
2. Refractory atrial fibrillation/flutter and/or with severe symptoms
3. Refractory sinus, atrial or junctional tachycardia and/or with severe symptoms
4. Idiopathic ventricular premature depolarization from the right ventricular outflow tract associated with severe symptoms
5. Monomorphic VT (can consider cases of polymorphic VT)
6. VF (uncommon indication)
7. PVC-induced cardiomyopathy

Contraindications are generally the same as for EPS (see prior section).

Pulmonary Vein Isolation (PVI) for the treatment of AF:

Indications, Technique, & Outcomes:

Indicated for patients with symptomatic AF who have either failed pharmacologic therapies for rhythm control or cannot tolerate medication side effects. Among patients with HFrEF and NYHA II-III symptoms with persistent AF who are chosen for a rhythm control strategy, PVI leads 36% absolute increase in AF-free survival at 24 months, 26% absolute reduction in unplanned hospitalizations, and a 10% absolute reduction in overall mortality with AF ablation as compared to amiodarone.

Can be accomplished with radiofrequency (RFA) or cryoablation. In patients with drug refractory, symptomatic paroxysmal AF, cryoablation is non-inferior, reduces procedural time, but increases fluoroscopy time as compared to RFA. The procedure aims to electrically isolate the antral portion of the pulmonary veins, a region identified as containing >90% of the ectopic beats involved in the generation and maintenance of AF. As a result, cavotricuspid isthmus line ablation can be performed during the same procedure if atrial flutter is co-occurring.

Efficacy at 1 year has been reported to be as high as 80-85% for paroxysmal AF but decreases to 50-60% for persistent AF.

Anticoagulation:

As with any cardioversion, there is a risk of thromboembolism with PVI. All patients should be on anticoagulation peri-procedurally. Patients with AF >48 hours should be on therapeutic anticoagulation for at least 3 weeks or have a TEE prior to PVI. Anticoagulation should continue for at least two months after the procedure, although based on patient wishes, risk factors/stratification, and aggressive post-ablation monitoring some EP physicians will choose to discontinue anticoagulation.

Complications:

1. Complete heart block
2. Thromboembolism
3. Cardiac tamponade
4. Acute MI
5. Pericarditis
6. Pulmonary vein stenosis
7. Phrenic nerve paralysis
8. Atrioesophageal fistula

References:

1. American Heart Association, American Heart Association, and American Heart Association. "guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) of pediatric and neonatal patients: neonatal resuscitation guidelines." *Pediatrics* 117.5 (2006): e1029-e1038
2. Jacobs, Ian, et al. "Part 6: defibrillation: 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations." *Circulation* 122.16_suppl_2 (2010): S325-S337
3. Lown, Bernard, Raghavan Amarasingham, and Jose Neuman. "New method for terminating cardiac arrhythmias: use of synchronized capacitor discharge." *JAMA* 256.5 (1986): 621-627
4. Knight, B. “Basic principles and techniques of cardioversion and defibrillation.” UpToDate 2018
5. Knight, B. “Cardioversion for specific arrhythmias.” UpToDate 2019
6. Kadish, Alan H., et al. "ACC/AHA clinical competence statement on electrocardiography and ambulatory electrocardiography: A report of the ACC/AHA/ACP–ASIM Task Force on Clinical Competence (ACC/AHA Committee to Develop a Clinical Competence Statement on Electrocardiography and Ambulatory Electrocardiography) Endorsed by the International Society for Holter and Noninvasive Electrocardiology." *Journal of the American College of Cardiology* 38.7 (2001): 2091-2100
7. Zipes, Douglas P., et al. "Guidelines for clinical intracardiac electrophysiological and catheter ablation procedures: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Intracardiac Electrophysiologic and Catheter Ablation Procedures), developed in collaboration with the North American Society of Pacing and Electrophysiology." *Journal of the American College of Cardiology* 26.2 (1995): 555-573
8. Homoud, M. “Invasive cardiac electrophysiology studies.” UpToDate 2019
9. Dagres, Nikolaos, et al. "Complications of atrial fibrillation ablation in a high-volume center in 1,000 procedures: Still cause for concern?." *Journal of cardiovascular electrophysiology* 20.9 (2009): 1014-1019
10. Haissaguerre, Michel, et al. "Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins." *New England Journal of Medicine* 339.10 (1998): 659-666
11. Oral, Hakan, et al. "Circumferential pulmonary-vein ablation for chronic atrial fibrillation." *New England Journal of Medicine*354.9 (2006): 934-941
12. Pappone, Carlo, and Vincenzo Santinelli. "Atrial fibrillation ablation: state of the art." *The American journal of cardiology*96.12 (2005): 59-64
13. Ganz, L. “Overview of catheter ablation of cardiac arrhythmias.” UpToDate 2019
14. Passman, R. “Catheter ablation to prevent recurrent atrial fibrillation.” UpToDate 2018
15. Kuck, Karl-Heinz, et al. "Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation." *New England Journal of Medicine* 374.23 (2016): 2235-2245
16. Di Biase, Luigi, et al. "Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial." *Circulation* 133.17 (2016): 1637-1644

Quick Reference Guide: Arrhythmias and Electrophysiology

Narrow Complex Tachycardia (NCT)

- If unstable with NCT ⇒ DCCV with following energy
  - Regular → 50-100J
  - Irregular → 120-200J biphasic or 200J monophasic
- The following table characterizes the NCTs by mechanism and location

LOCATION	MECHANISM: ↑ AUTOMATICITY	MECHANISM: RE-ENTRY
SINUS NODE	Sinus Tachycardia ● Secondary cause (HoTN, pain, fever, PE, CHF, acute MI, fistula, etc.) vs drug effect/toxicity/withdrawal ● HR 100-150 in older pts; up to 200 in younger pts ● Gradual onset ● Treat underlying cause	Sino-Atrial Nodal Reentrant Tachycardia ● Reentry within or around SA node ● Paroxysmal, abrupt on/off ● P wave morphology similar to baseline ● Treat w/ vagal maneuvers, Valsalva; nodal blockade; ablation
ATRIUM	Atrial Tachycardia ● Focal vs multifocal ● Atrial rate 100-250, vent rate 90-120 (variable block) ● Focal AT: Structural heart dz vs Dig toxicity; d/c Dig, rate control (BB vs CCB), ablation. ● MAT: ≥3 P-wave morphologies, a/w chronic pulmonary disease; prefer CCB > BB if severe lung disease	Atrial Flutter ● Macro-reentrant circuit ● Atrial rate 250-300, vent rate 150 (if 2:1 conduction) ● Slow and diagnose with vagal maneuvers ± adenosine ● Similar mgmt. to atrial fib: rate/rhythm control, anticoagulation ● Prefer BB, CCB, Dig to class 1A/1C meds → can enable 1:1 conduction ● Typical flutter is amenable to ablation
AV NODE	Non-Reentrant Junctional Tachycardia ● JET (junctional ectopic tach): infants > adults, particularly post-cardiac surgery for CHD; due to ectopic focus; high morbidity ● NPJT (non-paroxysmal JT): adults > children; “accelerated junctional rhythm”; a/w digoxin toxicity and acute MI; difficult to distinguish from AVNRT w/o EP study; treat underlying cause	AVNRT ● Reentry thru dual pathways in AV node ● Abrupt on/off, rates 150-220 ● Retrograde P, can be buried in QRS ● Acute: vagal, adenosine ● Mgmt: BB, CCB; ablation is definitive AVRT ● Reentry thru acc. pathway + AV node ● Narrow = orthodromic (antegrade thru AV node, retrograde thru acc. path); use nodal blockade ● Wide/pre-excitation = antidromic; avoid nodal blockade (see WCT chapter) ● Definitive tx: ablation

Wide Complex Tachycardia (WCT)

- Refers to rate > 100bpm and QRS ≥ 120ms
- The DDx for WCTs include
  - VT
  - SVT with aberrancy
  - SVT w/ pre-excitation, and
  - Pacemaker-related tachycardias
- The clinical presentation of WCT can be variable, from asymptomatic runs of NSVT to a patient who has coded. Because most patients do not tolerate VT for long periods of time, when you see WCT, assume it is VT feel for a pulse and obtain BP ASAP!
- Approach the initial management of WCT according to patient stability (as below). See chapter for more details on mgmt according to etiology
  - Pulseless: Immediately start the pulseless VT ACLS algorithm and prepare for **unsynchronized** DCCV
  - Hemodynamically unstable or highly symptomatic: Worry about etiology AFTER YOU'VE STABILIZED PATIENT
    - Prepare for **synchronized** DCCV (fentanyl/versed for sedation), put pads on the patient, and call for help (e.g. cardiology, EP, RICU, etc.)
    - Start amiodarone (150 mg x 1 Q 3–5 min, then drip @ 1 mg/min), and/or lidocaine (100 mg x 1, then drip @ 1–4 mg/min). Amiodarone typically is an appropriate anti-arrhythmic to start unless there is QT prolongation and concern or TdP
    - If regular, monomorphic, and there is some suspicion for SVT, you can consider using adenosine as both a diagnostic and therapeutic intervention
    - If pacemaker-mediated or tracked WCT→ apply magnet

Atrial Fibrillation (AF)

- Atrial fibrillation is the most common sustained cardiac rhythm disturbance, increasing in prevalence with age (0.4% to almost 20%)
- In general, AF results from an abnormal atrial response to reentry and/or rapid focal ectopic firing
- Patients can be asymptomatic, but many describe palpitations, fatigue, dyspnea, lightheadedness and diaphoresis
  - Thromboembolic CVA is the initial manifestation in 10–40% of patients
- TTE should be performed in all patients who present with new-onset AF in order to evaluate for a structural etiology. In addition, thyroid function testing should routinely be performed, as hyperthyroidism predisposes to AF. Also consider renal and liver function tests, as well as cardiac biomarkers (including troponin and NT-proBNP) based on clinical presentation
- Rate versus rhythm control: no mortality difference
- Anticoagulation: All patients with AF should be on anticoagulation except those at the lowest risk of thromboembolic stroke
  - The AHA/ACC 2019 guidelines recommend DOACs (including dabigatran, rivaroxaban, apixaban and edoxaban) over warfarin to reduce stroke risk in appropriate AFib patients, unless moderate-to-severe mitral stenosis or a mechanical heart valve

Temporary Pacing and Pacemaker Therapy

- Temporary pacing includes transcutaneous and transvenous pacing, both of which are indicated as urgent or emergent therapy in patients with hemodynamically significant bradyarrhythmia
- Transcutaneous pacing can be performed urgently without input from cardiology, but should involve the Senior ON and nursing supervisors
  - Short-acting sedation (e.g. with Dilaudid/Ativan) is indicated in non-ACLS setting (consider early involvement of Anesthesia)
  - Pace by turning defibrillator to "Pacer" mode; a good rule of thumb is to set the HR and output at a starting rate 100 bpm and 100 mA, respectively
- Transvenous pacing is a more durable option than transcutaneous pacing, and is often employed as a temporary bridge to recovery or to PPM placement
  - In contrast to placement of a temp wire for transvenous pacing must be performed in the cath lab
  - The pacing lead is inserted into the right ventricle via the right internal jugular, left subclavian, or femoral veins (less reliable and increased risk for dislodgement)
  - Temp wires may remain in place for up to 7-10 days but carry a risk of infection
  - Daily maintenance includes CXR, threshold testing, and ECG (all to assess for lead migration)
- Permanent pacing is indicated for irreversible symptomatic bradycardia, chronotropic incompetence, or unstable conduction disorders

- There are many different pacing modes, which are designated by a 1-5 letter code. In the chart below, "position" refers to letter position
    - As an example, in the 4-letter code DDDR, the D in position I implies that both chambers (the atria and the ventricles) can be paced, the D in position II indicates that both chambers (the atria and the ventricles) can be sensed, the D in position III indicates that the device can respond to sensing by either triggering activity or inhibiting itself, and the R in position IV indicates that the device allows for rate modulation

NASPE/BPEG Codes for Pacing Operating Modes			
Position I	**Position II**	**Position III**	**Position IV**
Chamber(s) Paced	Chamber(s) Sensed	Response to Sensing	Rate Modulation
O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T =Triggered	R = Rate Modulation
V = Ventricle	V = Ventricle	I = Inhibited	
D = Dual (A+V)	D = Dual (A+V)	D = Dual (A+V)	

Implantable Cardioverter-Defibrillator Therapy

- Per AHA/ACC guidelines, ICDs are indicated for both primary and second prevention in patients on optimal medical therapy who have an estimated survival of at least 1 year (with good functional status)
- Class I indications for secondary prevention include:
    - Survivors of cardiac arrest due to VF or sustained VT without reversible causes (AVID)
- Class I indications for primary prevention (with trial references) include:
    - Ischemic cardiomyopathy and LVEF ≤ 30-40% at least 40 days post-MI (DINAMIT) or at least 3 months post-CABG (CABG-PATCH)
    - LVEF ≤ 30% and NYHA Class I, II, or III (MADIT-II)
    - LVEF ≤ 35% and NYHA Class II or III (SCD-HeFT)
    - LVEF ≤ 40% and inducible VF or sustained VT at EP study (MUSTT)
    - Non-ischemic cardiomyopathy with at least 3 months of documented: CHF, LVEF ≤ 35%, and NYHA Class II or III (SCD-HeFT)
    - Syncope of unknown origin and VT/VF induced at EP study
    - Spontaneous sustained VT (+/- hemodynamic instability) with structural heart disease
- Wearable cardiac defibrillators (WCDs) are externally worn defibrillators, generally considered as interval therapy in patients awaiting ICD
    - The VEST Trail showed that among post-MI patients with EF ≤35%, WCDs did not reduce SCD and ventricular tachyarrhythmias but did reduce the secondary endpoint of all-cause mortality up to 90 days

Cardiac Resynchronization Therapy (CRT)

- Cardiac resynchronization therapy (CRT) devices have an RA, RV, and coronary sinus (epicardial pacing of LV) leads, allowing for optimization of A-V and V-V synchrony, which has been shown to improve stroke volume
    - Class I indications: CRT implantation is recommended for patients with chronic heart failure (NYHA function class II, and ambulatory IV) with LVEF ≤ 35% and LBBB w/ QRS duration > 150 ms and should be considered in these patients if QRS duration is 120-150 ms
    - CRT devices may only provide BiV pacing (CRT-P) or may allow for BiV pacing plus defibrillation with ICD function (CRT-D)

Procedures in EP and EP Studies

- Cardioversion (DCCV) and defibrillation are non-invasive interventions that can terminate tachyarrhythmias by delivering an electrical shock to the heart

- Emergent DCCV and defibrillation are generally indicated in cases of clinical instability. Planned DCCV may also be performed as an effective treatment for SVTs
- The delivered shock depolarizes all or most excitable cardiac tissue and induces a refractory period that terminates reentrant activity
- Cardioversion is performed by synchronizing the shock to a QRS complex (thus requires a rhythm in which the QRS complex is present) and restores sinus rhythm in 70–95% of patients. The procedure is as follows:

21. Turn the mode selector to DEFIB (red area). Select the desired energy using the up and down arrow keys in the front panel. In general:
    a. Narrow, regular: 50 – 100 J (atrial flutter often converts with 50 J)
    b. Narrow, irregular: 120 – 200 J (atrial fibrillation typically requires 150 J)
    c. Wide, regular: 100 J
    d. Wide, irregular: 150 – 200 J (defibrillation dose)
22. Press the Sync On/Off button
    a. Confirm that a Sync marker appears on the monitor above each detected R wave to indicate where discharge will occur
    b. If necessary, use the LEAD and SIZE buttons to establish settings that yield the best display
23. Press the CHARGE button on the front panel
24. Ensure all are clear from the bed then press and hold the illuminated SHOCK button on the front panel. The defibrillator will discharge with the next detected R wave
25. If additional shocks are necessary, increase the energy level as needed

- Defibrillation is unsynchronized and delivers a random shock during the cardiac cycle.

5. Turn the mode selector to DEFIB (red area)
    a. The unit displays DEFIB 120J SEL on the monitor
    b. The default energy selections for adult patients are Shock 1: 120J, Shock 2: 150J, Shock 3: 200J. You can use energy select (UP and DOWN arrow keys) to change settings
6. If the monitor shows a shockable rhythm, press the CHARGE button on the front panel. If patient is pulseless, continue CPR while charging
7. Ensure all are clear from the bed then press and hold the illuminated SHOCK button on the front panel
8. If patient is pulseless, resume CPR for 2 minutes before the next pulse and rhythm check

- An electrophysiology study (EPS) is an elective, invasive, intracardiac catheter-based intervention that measures specific intervals within the cardiac cycle. The purpose is to better understand the etiology, clinical significance, and management of brady-and tachy-arrhythmias
- A common procedure in EP is Pulmonary Vein Isolation (PVI), performed with either radiofrequency (RFA) or cryoablation, which involves electrical isolation of the antral portion of the pulmonary veins, which contains >90% of the ectopic beats involved in AFib.
  PVI is indicated in patients with symptomatic atrial fibrillation who have either failed pharmacologic therapies for rhythm control or cannot tolerate medication side effects. Importantly, ablation does not negate the need for therapeutic anticoagulation

Electrophysiology Studies and Procedures

The purpose of this section is to provide background/basic information on three commonly employed EP procedures: synchronized cardioversion and defibrillation, diagnostic EP studies, and catheter ablations.

Subsection 1 – Synchronized Cardioversion and Defibrillation

Subsection 2 – Electrophysiology Study (EPS)

Subsection 3 – Catheter Ablation Therapy

Synchronized Cardioversion and Defibrillation

Cardioversion (DCCV) and defibrillation are non-invasive interventions that can terminate tachyarrhythmias by delivering an electrical shock to the heart. Cardioversion is performed by synchronizing the shock to a QRS complex while defibrillation is unsynchronized and delivers a random shock during the cardiac cycle.

Indications and Contraindications

Emergent DCCV and defibrillation are indicated in cases of clinical instability. Elective DCCV may also be performed as an effective treatment for SVTs.

Table 1: Cardioversion & defibrillation indications and energy dosing

CARDIOVERSION	**Monophasic (J)**	**Biphasic (J)***
AVRT/AVNRT[1]	50-100	<50-100
Atrial flutter[2]	100	50-100
Atrial fibrillation[2]	200	120-200
VT (with pulse)	200	100
DEFIBRILLATION		
VT (pulseless)	360	150-200
VF	360	150-200

[1]includes reentry arrhythmias AVRT and AVNRT (attempt adenosine first)
[2]includes:

AF/AFL of ≥48h (or unknown) duration and anticoagulated for 3–4 weeks (INR 2–3)

AF/AFL of <48h duration, for which anticoagulation is optional depending on risk
AF/AFL of unknown duration with CHF and absence of thrombus in LA on TEE acute onset AF/AFL with hemodynamic compromise: MI, pulmonary edema, hypotension
*All MGH defibrillators are biphasic which are typically effective at lower energy levels. Large patients may be difficult to cardiovert/defibrillate even at 360 J biphasic.

In general, **DCCV/defibrillation is contraindicated in the following cases**:

1. Known atrial or ventricular thrombus without emergent indication
2. Unknown duration AF/AFL without anticoagulation (unless with TEE or emergent)
3. Rhythms associated with increased automaticity or triggered activity (MAT, junctional tachycardia, AIVR) which typically recur within seconds after shock, and the release of endogenous catecholamines from the shock may further exacerbate the arrhythmia.
4. Digitalis toxicity
5. Severe electrolyte imbalance

Additionally, the following considerations exist for these **special populations**:

1**. Patients who are pregnant**: Can be performed without affecting the rhythm of the fetus. Fetal heart rate monitoring during the procedure is recommended.

2. **Patients who have pacemakers/ICDs**: Can be performed but the electrode should be > 12 cm from the pulse generator and an anteroposterior electrode orientation is recommended. The pacemaker/ICD should be interrogated afterward to ensure proper functioning.

Mechanism and Procedure
The delivered shock depolarizes all or most excitable cardiac tissue and induces a refractory period that terminates reentrant activity. Cardioversion restores sinus rhythm in 70–95% of patients. Efficacy decreases with increased resistance (tissue density, physical distance due to habitus), prolonged arrhythmia duration, presence of structural heart disease, and involvement of multiple reentry circuits.

Step-by-step instructions for **emergent cardioversion and defibrillation:**
Cardioversion:

1. Turn the mode selector to DEFIB (red area). Select the desired energy using the up and down arrow keys in the front panel. See above for desired energy, or in general:
    a. Narrow, regular: 50 – 100 J (atrial flutter often converts with 50 J)
    b. Narrow, irregular: 120 – 200 J (atrial fibrillation typically requires 150 J)
    c. Wide, regular: 100 J
    d. Wide, irregular: 150 – 200 J (defibrillation dose)
2. Press the Sync On/Off button
    a. Confirm that a Sync marker appears on the monitor above each detected R wave to indicate where discharge will occur
    b. If necessary, use the LEAD and SIZE buttons to establish settings that yield the best display
3. Press the CHARGE button on the front panel
4. Ensure all are clear from the bed then press and hold the illuminated SHOCK button on the front panel. The defibrillator will discharge with the next detected R wave
5. If additional shocks are necessary, increase the energy level as needed

Defibrillation:

9. Turn the mode selector to DEFIB (red area)
    a. The unit displays DEFIB 120J SEL on the monitor
    b. The default energy selections for adult patients are Shock 1: 120J, Shock 2: 150J, Shock 3: 200J. You can use energy select (UP and DOWN arrow keys) to change settings
10. If the monitor shows a shockable rhythm, press the CHARGE button on the front panel. If patient is pulseless, continue CPR while charging
11. Ensure all are clear from the bed then press and hold the illuminated SHOCK button
12. If patient is pulseless, resume CPR for 2 minutes before the next pulse and rhythm check

For **non-emergent and routine procedures:** NPO for at least 6-8h. Some patients may require periprocedural anticoagulation to prevent thromboembolism. TEE is frequently used to look for the presence of a LA thrombus.

Complications: After shocking, ST & T wave changes may occur and typically resolve within 5 minutes. However, the following complications may also occur:

- **Arrhythmias/Conduction abnormalities**:
    - Self-limited and include sinus tachycardia, PAC, PVC, NSVT, VT, VF, and LBBB.
    - May cause hemodynamic instability requiring further intervention
- **Thromboembolism**: Approximately 1% with anticoagulation, 5% without anticoagulation
- **Myocardial necrosis**: Severity depends on strength and number of shocks delivered
- **Myocardial dysfunction/stunning**:
    - Global LV dysfunction can be present until 48 hours after shock
    - Interpret cardiac studies within this 48h window with caution
- **Pulmonary edema**: Rare complication seen in patients with AF and/or LV dysfunction
- **Hypotension:** Transient, may last several hours, typically fluid-responsive
- **Cutaneous burns**:
    - Seen in 20-25% of patients
    - May use prophylactic steroid cream or topical NSAIDs at the site of electrodes

Electrophysiology Study (EPS)

EPS is an elective, invasive, intracardiac catheter-based intervention that measures specific intervals within the cardiac cycle to better understand the etiology, clinical significance, and management of brady- and tachy-arrhythmias.

Indications:

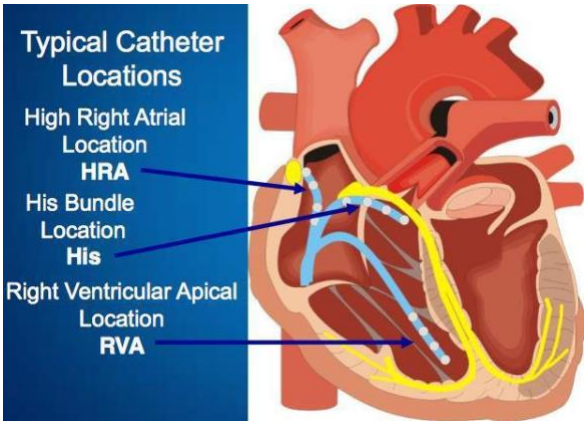
6. **Bradyarrhythmias**: acquire corroborative data in symptomatic patients with episodic bradyarrhythmia or define level of AV conduction abnormality
7. **Tachyarrhythmias**: define mechanism of NCT or WCT or reproduce a clinically defined tachycardia for mapping and ablation
8. **ICD implantation and programming**: search for EPS-induced VT or VF in patients with structural heart disease, NSVT, or reduced LVEF to justify ICD implantation and define optimal ICD parameters
9. **Syncope of unknown etiology**: to assess SN function, AV conduction, and search for VT/VF in patients with syncope and organic heart disease
10. **After cardiac surgery**: to assess the effect of cardiac surgery on arrhythmia risk

Contraindications: active ACS, bacteremia, ADHF (not caused by the arrhythmia), critical AS, severe HOCM, severe left main or 3-vessel CAD, presence of a major bleeding diathesis, presence of an acute lower extremity DVT (if femoral vein cannulation is required).

Mechanism and Procedure

Performed in the EP lab and patients are given at least conscious sedation. Standard ECG leads and defibrillation pads are applied. Multiple sites of venous (and at times, arterial) access are acquired for intracardiac catheter placement. Femoral access is most common. Catheters with electrode tips are placed in specific locations to both pace and record.

- High right atrium: Reflects SA node function, conduction, and direction of atrial activation
- Coronary sinus: Reflects LA activation. AV patients with SVT or pre-excitation
- Tricuspid annulus (His): Tracings from low Obtained in His bundle, and high septal RV depolarization septal RA, bundle activity reflect His
- RV apex: Reflects RV activity
- Left heart (via **transseptal or retrograde approach** for mapping/ablation) **aortic**



Mapping

At the conclusion of the diagnostic EPS, a subset of patients may undergo additional mapping and ablation for treatment of an arrhythmia. The created “map” is used to guide and localize potential ablation sites. Mapping prior to ablation is not necessary for certain types of arrhythmias that have a defined anatomical course (i.e. typical atrial flutter).

Catheter Ablation Therapy

Indications

1. WPW, accessory pathway-mediated, and other variant pre-excitation states
2. Refractory atrial fibrillation/flutter and/or with severe symptoms
3. Refractory sinus, atrial or junctional tachycardia and/or with severe symptoms
4. Idiopathic ventricular premature depolarization from the right ventricular outflow tract associated with severe symptoms
5. Monomorphic VT (can consider cases of polymorphic VT)
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Contraindications are generally the same as for EPS (see prior section).

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Indications, Technique, & Outcomes:

Indicated for patients with symptomatic AF who have either failed pharmacologic therapies for rhythm control or cannot tolerate medication side effects. Among patients with HFrEF and NYHA II-III symptoms with persistent AF who are chosen for a rhythm control strategy, PVI leads 36% absolute increase in AF-free survival at 24 months, 26% absolute reduction in unplanned hospitalizations, and a 10% absolute reduction in overall mortality with AF ablation as compared to amiodarone.

Can be accomplished with radiofrequency (RFA) or cryoablation. In patients with drug refractory, symptomatic paroxysmal AF, cryoablation is non-inferior, reduces procedural time, but increases fluoroscopy time as compared to RFA. The procedure aims to electrically isolate the antral portion of the pulmonary veins, a region identified as containing >90% of the ectopic beats involved in the generation and maintenance of AF. As a result, cavotricuspid isthmus line ablation can be performed during the same procedure if atrial flutter is co-occurring.

Efficacy at 1 year has been reported to be as high as 80-85% for paroxysmal AF but decreases to 50-60% for persistent AF.

Anticoagulation:

As with any cardioversion, there is a risk of thromboembolism with PVI. All patients should be on anticoagulation peri-procedurally. Patients with AF >48 hours should be on therapeutic anticoagulation for at least 3 weeks or have a TEE prior to PVI. Anticoagulation should continue for at least two months after the procedure, although based on patient wishes, risk factors/stratification, and aggressive post-ablation monitoring some EP physicians will choose to discontinue anticoagulation.

Complications:

1. Complete heart block
2. Thromboembolism
3. Cardiac tamponade
4. Acute MI
5. Pericarditis
6. Pulmonary vein stenosis
7. Phrenic nerve paralysis
8. Atrioesophageal fistula

References:

17. American Heart Association, American Heart Association, and American Heart Association. "guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) of pediatric and neonatal patients: neonatal resuscitation guidelines." *Pediatrics* 117.5 (2006): e1029-e1038
18. Jacobs, Ian, et al. "Part 6: defibrillation: 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations." *Circulation* 122.16_suppl_2 (2010): S325-S337
19. Lown, Bernard, Raghavan Amarasingham, and Jose Neuman. "New method for terminating cardiac arrhythmias: use of synchronized capacitor discharge." *JAMA* 256.5 (1986): 621-627
20. Knight, B. “Basic principles and techniques of cardioversion and defibrillation.” UpToDate 2018
21. Knight, B. “Cardioversion for specific arrhythmias.” UpToDate 2019
22. Kadish, Alan H., et al. "ACC/AHA clinical competence statement on electrocardiography and ambulatory electrocardiography: A report of the ACC/AHA/ACP–ASIM Task Force on Clinical Competence (ACC/AHA Committee to Develop a Clinical Competence Statement on Electrocardiography and Ambulatory Electrocardiography) Endorsed by the International Society for Holter and Noninvasive Electrocardiology." *Journal of the American College of Cardiology* 38.7 (2001): 2091-2100
23. Zipes, Douglas P., et al. "Guidelines for clinical intracardiac electrophysiological and catheter ablation procedures: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Intracardiac Electrophysiologic and Catheter Ablation Procedures), developed in collaboration with the North American Society of Pacing and Electrophysiology." *Journal of the American College of Cardiology* 26.2 (1995): 555-573
24. Homoud, M. “Invasive cardiac electrophysiology studies.” UpToDate 2019
25. Dagres, Nikolaos, et al. "Complications of atrial fibrillation ablation in a high-volume center in 1,000 procedures: Still cause for concern?." *Journal of cardiovascular electrophysiology* 20.9 (2009): 1014-1019
26. Haissaguerre, Michel, et al. "Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins." *New England Journal of Medicine* 339.10 (1998): 659-666
27. Oral, Hakan, et al. "Circumferential pulmonary-vein ablation for chronic atrial fibrillation." *New England Journal of Medicine*354.9 (2006): 934-941
28. Pappone, Carlo, and Vincenzo Santinelli. "Atrial fibrillation ablation: state of the art." *The American journal of cardiology*96.12 (2005): 59-64
29. Ganz, L. “Overview of catheter ablation of cardiac arrhythmias.” UpToDate 2019
30. Passman, R. “Catheter ablation to prevent recurrent atrial fibrillation.” UpToDate 2018
31. Kuck, Karl-Heinz, et al. "Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation." *New England Journal of Medicine* 374.23 (2016): 2235-2245
32. Di Biase, Luigi, et al. "Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial." *Circulation* 133.17 (2016): 1637-1644

Quick Reference Guide: Arrhythmias and Electrophysiology

Narrow Complex Tachycardia (NCT)

- If unstable with NCT ⇒ DCCV with following energy
  - Regular → 50-100J
  - Irregular → 120-200J biphasic or 200J monophasic
- The following table characterizes the NCTs by mechanism and location

LOCATION	MECHANISM: ↑ AUTOMATICITY	MECHANISM: RE-ENTRY
SINUS NODE	Sinus Tachycardia ● Secondary cause (HoTN, pain, fever, PE, CHF, acute MI, fistula, etc.) vs drug effect/toxicity/withdrawal ● HR 100-150 in older pts; up to 200 in younger pts ● Gradual onset ● Treat underlying cause	Sino-Atrial Nodal Reentrant Tachycardia ● Reentry within or around SA node ● Paroxysmal, abrupt on/off ● P wave morphology similar to baseline ● Treat w/ vagal maneuvers, Valsalva; nodal blockade; ablation
ATRIUM	Atrial Tachycardia ● Focal vs multifocal ● Atrial rate 100-250, vent rate 90-120 (variable block) ● Focal AT: Structural heart dz vs Dig toxicity; d/c Dig, rate control (BB vs CCB), ablation. ● MAT: ≥3 P-wave morphologies, a/w chronic pulmonary disease; prefer CCB > BB if severe lung disease	Atrial Flutter ● Macro-reentrant circuit ● Atrial rate 250-300, vent rate 150 (if 2:1 conduction) ● Slow and diagnose with vagal maneuvers ± adenosine ● Similar mgmt. to atrial fib: rate/rhythm control, anticoagulation ● Prefer BB, CCB, Dig to class 1A/1C meds → can enable 1:1 conduction ● Typical flutter is amenable to ablation
AV NODE	Non-Reentrant Junctional Tachycardia ● JET (junctional ectopic tach): infants > adults, particularly post-cardiac surgery for CHD; due to ectopic focus; high morbidity ● NPJT (non-paroxysmal JT): adults > children; “accelerated junctional rhythm”; a/w digoxin toxicity and acute MI; difficult to distinguish from AVNRT w/o EP study; treat underlying cause	AVNRT ● Reentry thru dual pathways in AV node ● Abrupt on/off, rates 150-220 ● Retrograde P, can be buried in QRS ● Acute: vagal, adenosine ● Mgmt: BB, CCB; ablation is definitive AVRT ● Reentry thru acc. pathway + AV node ● Narrow = orthodromic (antegrade thru AV node, retrograde thru acc. path); use nodal blockade ● Wide/pre-excitation = antidromic; avoid nodal blockade (see WCT chapter) ● Definitive tx: ablation

Wide Complex Tachycardia (WCT)

- Refers to rate > 100bpm and QRS ≥ 120ms
- The DDx for WCTs include
  - VT
  - SVT with aberrancy
  - SVT w/ pre-excitation, and
  - Pacemaker-related tachycardias
- The clinical presentation of WCT can be variable, from asymptomatic runs of NSVT to a patient who has coded. Because most patients do not tolerate VT for long periods of time, when you see WCT, assume it is VT feel for a pulse and obtain BP ASAP!
- Approach the initial management of WCT according to patient stability (as below). See chapter for more details on mgmt according to etiology
  - Pulseless: Immediately start the pulseless VT ACLS algorithm and prepare for unsynchronized DCCV
  - Hemodynamically unstable or highly symptomatic: Worry about etiology AFTER YOU'VE STABILIZED PATIENT
    - Prepare for synchronized DCCV (fentanyl/versed for sedation), put pads on the patient, and call for help (e.g. cardiology, EP, RICU, etc.)
    - Start amiodarone (150 mg x 1 Q 3–5 min, then drip @ 1 mg/min), and/or lidocaine (100 mg x 1, then drip @ 1–4 mg/min). Amiodarone typically is an appropriate anti-arrhythmic to start unless there is QT prolongation and concern or TdP
    - If regular, monomorphic, and there is some suspicion for SVT, you can consider using adenosine as both a diagnostic and therapeutic intervention
    - If pacemaker-mediated or tracked WCT→ apply magnet

Atrial Fibrillation (AF)

- Atrial fibrillation is the most common sustained cardiac rhythm disturbance, increasing in prevalence with age (0.4% to almost 20%)
- In general, AF results from an abnormal atrial response to reentry and/or rapid focal ectopic firing
- Patients can be asymptomatic, but many describe palpitations, fatigue, dyspnea, lightheadedness and diaphoresis
  - Thromboembolic CVA is the initial manifestation in 10–40% of patients
- TTE should be performed in all patients who present with new-onset AF in order to evaluate for a structural etiology. In addition, thyroid function testing should routinely be performed, as hyperthyroidism predisposes to AF. Also consider renal and liver function tests, as well as cardiac biomarkers (including troponin and NT-proBNP) based on clinical presentation
- Rate versus rhythm control: no mortality difference
- Anticoagulation: All patients with AF should be on anticoagulation except those at the lowest risk of thromboembolic stroke
  - The AHA/ACC 2019 guidelines recommend DOACs (including dabigatran, rivaroxaban, apixaban and edoxaban) over warfarin to reduce stroke risk in appropriate AFib patients, unless moderate-to-severe mitral stenosis or a mechanical heart valve

Temporary Pacing and Pacemaker Therapy

- Temporary pacing includes transcutaneous and transvenous pacing, both of which are indicated as urgent or emergent therapy in patients with hemodynamically significant bradyarrhythmia
- Transcutaneous pacing can be performed urgently without input from cardiology, but should involve the Senior ON and nursing supervisors
  - Short-acting sedation (e.g. with Dilaudid/Ativan) is indicated in non-ACLS setting (consider early involvement of Anesthesia)
  - Pace by turning defibrillator to "Pacer" mode; a good rule of thumb is to set the HR and output at a starting rate 100 bpm and 100 mA, respectively
- Transvenous pacing is a more durable option than transcutaneous pacing, and is often employed as a temporary bridge to recovery or to PPM placement
  - In contrast to placement of a temp wire for transvenous pacing must be performed in the cath lab
  - The pacing lead is inserted into the right ventricle via the right internal jugular, left subclavian, or femoral veins (less reliable and increased risk for dislodgement)
  - Temp wires may remain in place for up to 7-10 days but carry a risk of infection
  - Daily maintenance includes CXR, threshold testing, and ECG (all to assess for lead migration)

- Permanent pacing is indicated for irreversible symptomatic bradycardia, chronotropic incompetence, or unstable conduction disorders
- There are many different pacing modes, which are designated by a 1-5 letter code. In the chart below, "position" refers to letter position
    - As an example, in the 4-letter code DDDR, the D in position I implies that both chambers (the atria and the ventricles) can be paced, the D in position II indicates that both chambers (the atria and the ventricles) can be sensed, the D in position III indicates that the device can respond to sensing by either triggering activity or inhibiting itself, and the R in position IV indicates that the device allows for rate modulation

NASPE/BPEG Codes for Pacing Operating Modes			
Position I	**Position II**	**Position III**	**Position IV**
Chamber(s) Paced	Chamber(s) Sensed	Response to Sensing	Rate Modulation
O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T =Triggered	R = Rate Modulation
V = Ventricle	V = Ventricle	I = Inhibited	
D = Dual (A+V)	D = Dual (A+V)	D = Dual (A+V)	

Implantable Cardioverter-Defibrillator Therapy

- Per AHA/ACC guidelines, ICDs are indicated for both primary and second prevention in patients on optimal medical therapy who have an estimated survival of at least 1 year (with good functional status)
- Class I indications for secondary prevention include:
    - Survivors of cardiac arrest due to VF or sustained VT without reversible causes (AVID)
- Class I indications for primary prevention (with trial references) include:
    - Ischemic cardiomyopathy and LVEF ≤ 30-40% at least 40 days post-MI (DINAMIT) or at least 3 months post-CABG (CABG-PATCH)
    - LVEF ≤ 30% and NYHA Class I, II, or III (MADIT-II)
    - LVEF ≤ 35% and NYHA Class II or III (SCD-HeFT)
    - LVEF ≤ 40% and inducible VF or sustained VT at EP study (MUSTT)
    - Non-ischemic cardiomyopathy with at least 3 months of documented: CHF, LVEF ≤ 35%, and NYHA Class II or III (SCD-HeFT)
    - Syncope of unknown origin and VT/VF induced at EP study
    - Spontaneous sustained VT (+/- hemodynamic instability) with structural heart disease
- Wearable cardiac defibrillators (WCDs) are externally worn defibrillators, generally considered as interval therapy in patients awaiting ICD
    - The VEST Trail showed that among post-MI patients with EF ≤35%, WCDs did not reduce SCD and ventricular tachyarrhythmias but did reduce the secondary endpoint of all-cause mortality up to 90 days

Cardiac Resynchronization Therapy (CRT)

- Cardiac resynchronization therapy (CRT) devices have an RA, RV, and coronary sinus (epicardial pacing of LV) leads, allowing for optimization of A-V and V-V synchrony, which has been shown to improve stroke volume
    - Class I indications: CRT implantation is recommended for patients with chronic heart failure (NYHA function class II, and ambulatory IV) with LVEF ≤ 35% and LBBB w/ QRS duration > 150 ms and should be considered in these patients if QRS duration is 120-150 ms
    - CRT devices may only provide BiV pacing (CRT-P) or may allow for BiV pacing plus defibrillation with ICD function (CRT-D)

Procedures in EP and EP Studies

- Cardioversion (DCCV) and defibrillation are non-invasive interventions that can terminate tachyarrhythmias by delivering an electrical shock to the heart
- Emergent DCCV and defibrillation are generally indicated in cases of clinical instability. Planned DCCV may also be performed as an effective treatment for SVTs
- The delivered shock depolarizes all or most excitable cardiac tissue and induces a refractory period that terminates reentrant activity
- Cardioversion is performed by synchronizing the shock to a QRS complex (thus requires a rhythm in which the QRS complex is present) and restores sinus rhythm in 70–95% of patients. The procedure is as follows:
    6. Turn the mode selector to DEFIB (red area). Select the desired energy using the up and down arrow keys in the front panel. In general:
        a. Narrow, regular: 50 – 100 J (atrial flutter often converts with 50 J)
        b. Narrow, irregular: 120 – 200 J (atrial fibrillation typically requires 150 J)
        c. Wide, regular: 100 J
        d. Wide, irregular: 150 – 200 J (defibrillation dose)
    7. Press the Sync On/Off button
        a. Confirm that a Sync marker appears on the monitor above each detected R wave to indicate where discharge will occur
        b. If necessary, use the LEAD and SIZE buttons to establish settings that yield the best display
    8. Press the CHARGE button on the front panel
    9. Ensure all are clear from the bed then press and hold the illuminated SHOCK button on the front panel. The defibrillator will discharge with the next detected R wave
    10. If additional shocks are necessary, increase the energy level as needed
- Defibrillation is unsynchronized and delivers a random shock during the cardiac cycle.
    13. Turn the mode selector to DEFIB (red area)
        a. The unit displays DEFIB 120J SEL on the monitor
        b. The default energy selections for adult patients are Shock 1: 120J, Shock 2: 150J, Shock 3: 200J. You can use energy select (UP and DOWN arrow keys) to change settings
    14. If the monitor shows a shockable rhythm, press the CHARGE button on the front panel. If patient is pulseless, continue CPR while charging
    15. Ensure all are clear from the bed then press and hold the illuminated SHOCK button on the front panel
    16. If patient is pulseless, resume CPR for 2 minutes before the next pulse and rhythm check
- An electrophysiology study (EPS) is an elective, invasive, intracardiac catheter-based intervention that measures specific intervals within the cardiac cycle. The purpose is to better understand the etiology, clinical significance, and management of brady-and tachy-arrhythmias
- A common procedure in EP is Pulmonary Vein Isolation (PVI), performed with either radiofrequency (RFA) or cryoablation, which involves electrical isolation of the antral portion of the pulmonary veins, which contains >90% of the ectopic beats involved in AFib.
  PVI is indicated in patients with symptomatic atrial fibrillation who have either failed pharmacologic therapies for rhythm control or cannot tolerate medication side effects. Importantly, ablation does not negate the need for therapeutic anticoagulation

VALVULAR HEART DISEASE

Aortic Stenosis (AS)

Epidemiology / Natural History

- **Incidence:** 0.2% in patients aged 50-59 years, but increases to 9.8% at age 80-89
- Bicuspid aortic valve incidence worldwide is 0.5–2%, but accounts for **50% of severe AS requiring AVR**
- Following diagnosis, the aortic valve area **decreases by ~ 0.1 cm² per year**, although can be highly variable
- Once symptoms develop, the average survival in patients with severe AS is 1-3 years. If the aortic valve is replaced, however, average survival returns to that of the general population.

Etiology: clinical risk factors for calcific AS mirror risk factors for CAD.

- AS is more common in men, advanced age, CKD (in part related to metastatic calcification), and vascular disease
- **Rheumatic heart disease** is responsible for the majority of cases in the developing world.
- **Radiation-induced valve disease** is increasingly recognized after mediastinal radiation therapy
- **Aortic sclerosis,** or calcification of the valve with no hemodynamic effects, is increasingly common with age, though over 5 years, only 10-15% of these patients will develop AS.

Pathophysiology: Left sided pressure changes

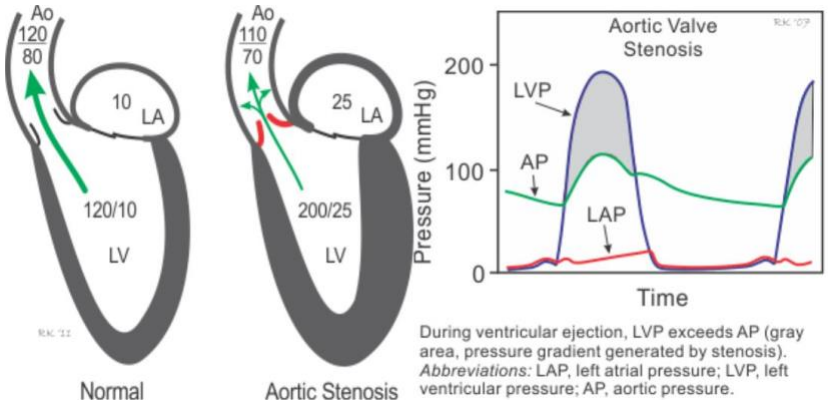


Figure 1. Aortic Stenosis. *CVPhysiology.com.* Note increased LVEDP, LA pressures and decreased systemic pressures.

Presentation:

- Symptoms generally occur only in severe AS; LV remodeling often precedes symptom onset**Angina:** results from several mechanisms including increased total LV oxygen demand in setting of LV hypertrophy, decreased coronary perfusion gradient due to elevated LVEDP, reduced diastolic perfusion time during tachycardia (later AS); ~ 50% of angina in AS have CAD
- **Syncope**: exercise-induced decrease in total peripheral resistance is uncompensated because CO is restricted by stenotic valve. 15% present with syncope.
- **Heart failure**: LV hypertrophy from chronic afterload results in diastolic dysfunction and/or systolic dysfunction

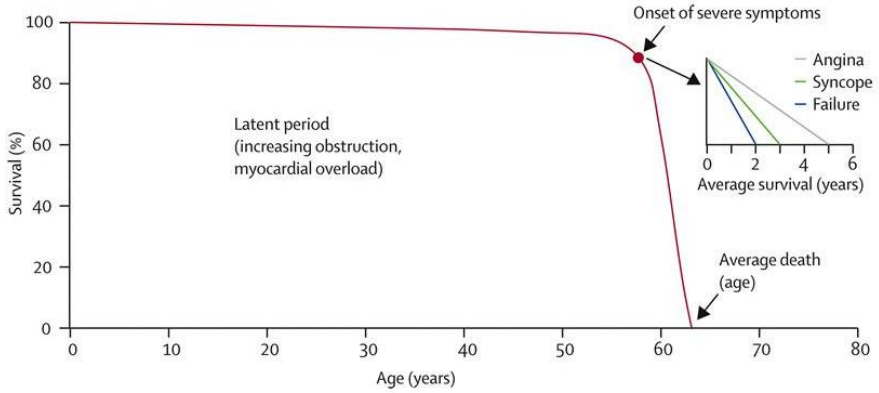


Figure 2. The natural history and rate of progression in aortic stenosis.[1]

Initial Clinical Evaluation

- Physical exam findings:

- Systolic ejection murmur at the R upper sternal border that radiates to the neck; occasionally a different quality of murmur which radiates to the apex (Gallavardin phenomenon).
- Decreases with maneuvers that decrease preload, such as standing and Valsalva. The severity of valvular disease may not correlate with the intensity of the murmur.
- Indicators of severe AS include a late-peaking murmur, delayed carotid upstroke (pulsus parvus et tardus), radiation to the left clavicle, and obliteration of the A2 component of S2.

- Diagnostics
  - **EKG** may show LVH, LAE, LAFB or LBBB
  - **Transthoracic echocardiography (TTE)** is used to evaluate valve anatomy and structure, valve gradients, and LV structure and function. Multiple views can show reduced leaflet excursion with a small aortic orifice. Short axis views "en-face" to the valve can demonstrate a bicuspid valve. Doppler echocardiography permits measurement of jet velocity and calculation of the LV-Aortic gradient, which are the standard parameters used for evaluation of severity (See Table 1).
  - **Cardiac catheterization** may be indicated for hemodynamic assessment if clinical and echo data are inconclusive or to evaluate for CAD prior to aortic valve replacement.
  - Particularly for patients with suspected LFLG severe AS, **need to optimized blood pressure control prior to diagnostic studies** to accurately assess AS severity

Grading AS Severity
Echocardiographic criteria (Table 1).

Table 1: 2020 ACC/AHA guidelines for grading of severity in aortic stenosis

	Valve area (cm^2)	Mean gradient (mmHg)	Jet velocity (m/s)
Mild	> 1.5	< 20	2.0-2.9
Moderate	1.0–1.5	20-39	3.0–3.9
Severe	< 1.0	> 40	> 4.0
Severe LFLG (reduced LVEF)	< 1.0	<40	<4 at rest ≥4 w/ dobut. stress echo

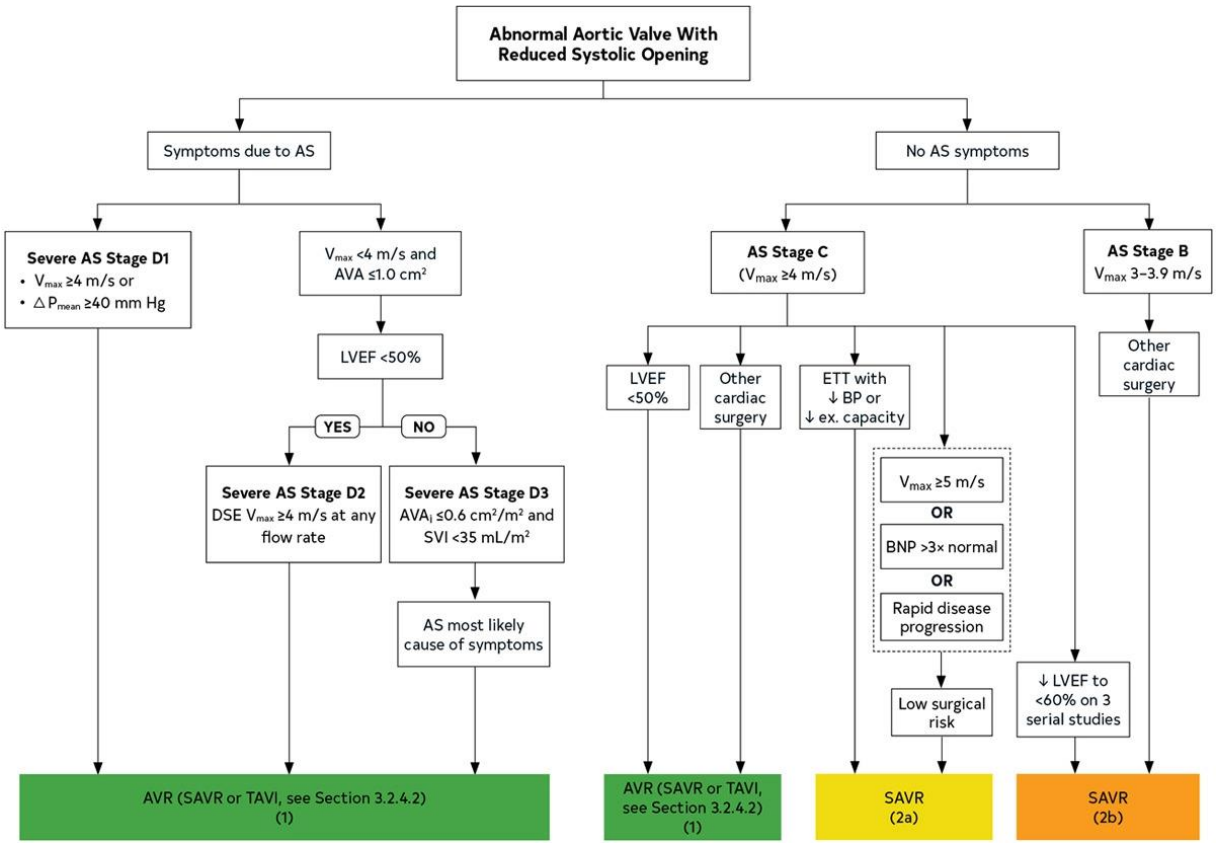
Clinical progression is separated into stages A-D. Patients with bicuspid aortic valve or valvular sclerosis are termed Stage A, or "at risk." Mild-to-moderate AS defines Stage B, or "progressive AS." Patients with Severe AS may be categorized as Stage C (asymptomatic) or Stage D (symptomatic).

Aortic Valve Replacement (AVR)
Determining indications for valve replacement is based on (1) presence of symptoms (2) severity of TTE criteria and (3) LV function. AVR is indicated in the following cases:

- **Symptomatic severe AS (Stage D):**
  - These patients require prompt AVR due to risk of sudden death. Exercise testing is contraindicated.
- **Asymptomatic, severe AS (Stage C2):**
  - Asymptomatic, severe AS with LVEF <50% have class I indication for AVR
  - Normal LVEF: exercise stress testing can be useful in asymptomatic patients to confirm lack of symptoms and evaluate physiologic change. If symptoms are provoked with exercise, patient is considered symptomatic and AVR is indicated. If poor exercise tolerance or fall in systolic pressure by ≥10 mmHg, AVR can be considered.

- **Low Flow Low Gradient AS**:
  In patients with reduced LV function (either from long-standing AS or concomitant systolic dysfunction), the gradient across the valve may be lower than expected (<40 mmHg) despite AVA <1 cm^2
  - Evaluation of LFLG AS is via dobutamine stress echo
    - In LFLG AS, the mean AV gradient should increase to >40mmHg or increase Vmax > 4m/s when the heart function is augmented with dobutamine. **AVR is indicated in these patients.**
    - Some patients fail to show an increase in stroke volume by ≥20% with dobutamine, referred to as "lack of contractile reserve"

    - Conversely, a normal valve may appear to have a low area if the ejection fraction and the flow across it are low (so termed "pseudo-severe" AS).
      - In "pseudo-severe" AS, the increased cardiac output may "stent" open the valve, and increase calculated aortic valve area (to an AVA >1cm2), while the mean AV gradient does not change or may even be reduced. **AVR is NOT indicated in these patients**



Medical Management

Only AVR has been shown to improve symptoms and mortality in AS patients. Guidelines for medical management involve treatment of HTN in patients at risk of developing AS (stage A) or with asymptomatic AS (stages B and C).

- **Hypertension**: Reduces the "double load" of afterload related to both the stenotic valve and systemic vasculature. No optimal regimen. ACEi may reduce fibrosis; caution as diuretics can reduce preload and CO, vasodilators can reduce coronary perfusion, and BB can reduce myocardial contractility. Up-titrate cautiously.
- **Volume status:** Volume status can be difficult to optimize in hospitalized patients with severe aortic stenosis. Adequate preload is necessary to ensure sufficient cardiac output. Nitrates and diuretics should be used with caution to avoid rapidly decreasing preload. High afterload can further potentiate high wall tension and diastolic dysfunction, resulting in flash pulmonary edema. Initial management of hypovolemia in patients with severe AS may require small fluid boluses (250cc) with careful monitoring of respiratory status. Patients with severe stenosis may easily "tip over" with volume overload and can rapidly experience pulmonary edema.
- **Statin therapy:** has not been shown to reduce progression of AS and therefore is not indicated for prevention of hemodynamic progression of AS.

Interventional Management:

- **Bioprosthethic vs mechanical valve**: depends on age (if <50, mechanical preferred for durability), contraindications to anticoagulation (required lifelong for mechanical valve), and surgical risk (mechanical valve only done surgically)
- **TAVR versus SAVR**: Recommendation of transcatheter AVR versus surgical AVR is made in multi-disciplinary consultation between surgery and structural cardiology.
  - Use of the Society of Thoracic Surgeons (STS score) risk calculator is helpful in determining surgical risk. An STS score <4% qualifies as low risk, 4-8 % as intermediate risk, >8% as high risk
    - Main risk factors that are *not included* in STS risk score are frailty, pulmonary hypertension, liver disease, and porcelain aorta. Consider these in addition to STS.

  TAVR was initially shown to be effective in patients with prohibitively high surgical risk (PARTNER trial), but has since been shown to be **non-inferior to surgical AVR** in patients with:
    - High surgical risk (PARTNER 1A, CoreValve trials), intermediate and low surgical risk (PARTNER-2, PARTNER-3, SURTAVI, NOTION, STACCATO, Siontis GCM trials)

  - TAVR has a slightly lower mortality risk and is associated with a shorter hospital length of stay, more rapid return to normal activities, lower risk of transient or permanent AF, less bleeding, and less pain than SAVR. However, it does have a higher risk of paravalvular leak, valve reintervention, and need for permanent pacemaker (PARTNER 3, NOTION)

Preparing a patient for TAVR and Periprocedural Considerations

- **To begin the process,** consult structural cardiology, cardiac surgery. Patients should have a recent TTE, a TAVR-protocol cardiac CT, and have undergone dental clearance (Panorex).
- Steps of Procedure for Percutaneous Route (most commonly transfemoral)
  - Femoral artery access obtained using a 14F sheath or greater
  - Transvenous access obtained and RV pacing wire placed
  - Cross the aortic valve with a guide wire and balloon dilation performed
  - With prosthetic valve in place (with fluoro +TEE or TTE guidance), rapid ventricular pacing (>180bpm) is used to decrease stroke volume and allow valve to be deployed.
  - Should immediately see reduction in transvalvular gradient
- Periprocedural considerations
  - Access:
    - **Bleeding:** Large bore sheaths and access sites and distal pulses (often with PVRs) require frequent monitoring, and patients are heparinized during the procedure followed by DAPT so at high risk for bleeding.
      - Complications include: retroperitoneal hemorrhage, femoral or iliac artery dissection, and development of femoral pseudoaneurysm. The major bleeding rates have decreased over the years with newer generation valves and catheters (~4% in the TVT registry)
  - Hemodynamics:
    - **Hypertension:** Due to sudden reduction in obstruction after TAVR; can often be controlled with IV pushes of vasodilators (i.e. hydralazine) PRN, though occasionally will require drips
    - **Hypotension:** Due to decreased preload. Left ventricular hypertrophy and diastolic heart disease means patients are usually volume responsive, so gentle fluid resuscitation should be attempted. Target a mean arterial pressure of 60-80.
  - Rhythm:
    - **High degree AV block**: Occurs more often in patients who have baseline conduction abnormalities (particularly RBBB) and those who are receiving self-expanding valves (ie Corevalve). In those cases, temporary pacing wires are left in place. Risk of PPM ~8% in the Siontis GCM metanalysis.

Antithrombotic Management Post-Valve Replacement

The incidence of transcatheter heart valve (THV) thrombosis following TAVR is 7% (majority subclinical), with larger valve size predisposing to higher rates of thrombosis.[7] The risk of stroke or TIA is greatest in the first 24 hours postoperatively and neurologic events peak in the first week.[8] Emerging data also suggests that there may be a role for intraoperative neuroprotective strategies given reports of changes in cognition in the post-TAVR period. Guidelines for anticoagulation after AVR (institutional preferences may vary, check with structural team, surgeon and/or fellow/attending):

- SAVR
  - Bioprosthetic AVR:
    - ASA 81 mg, 3-6 month of Coumadin for INR 2–3 after surgery. (Consider lifetime if AF, EF<30–35%, prior clot, hypercoagulable)
    - Stop Coumadin 48–72 hours before procedure, restart 24h afterwards
  - Mechanical AVR:
    - ASA 81 mg, INR 2–3 for life; if other risks factors (EF < 30%, AFib, prior clot, procoagulable disorder, Starr-Edwards Valve), INR goal 2.5–3.5.
    - IV heparin when INR < 2
  - If reversal of anticoagulation is urgent, FFP can be used (Class II), and is preferred over Vitamin K since it is thought to reduce the incidence of thrombotic complications (data is limited)
- TAVR
  - ASA 81 mg monotherapy is recommended, unless there is a concurrent indication for DAPT(i.e. recent PCI)
    - Aspirin monotherapy is non-inferior to DAPT for composite thrombotic events and associated with less bleeding (NEJM 2020; 383:1447-1457)
  - If patient has separate indication for anticoagulation (i.e. AFib) and no concurrent indication for antiplatelet therapy, they should be continued on the anticoagulant post-TAVR without addition of aspirin
    - GALILEO trial was stopped early due to higher rate of adverse events in Rivaroxiban + aspirin group

References:

1. Lester SJ et al. The natural history and progression of aortic stenosis. Chest. 1998;113(4):1109-14
2. Makkar RR et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med. 2012;366(18):1696-704
3. Kodali SK et al. Two-year outcomes after transcatheter or surgical aortic-value replacement. N Engl J Med. 2012;366(18):1686-95

4. Adams DH et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med. 2014;370(19):1790-8
5. Popma JJ et al. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk of surgery. J Am Coll Cardiol. 2014;63(19):1972-81
6. Leon MB et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2016;374(17):1609-20
7. Hansson NC et al. Transcatheter aortic valve thrombosis: Incidence, predisposing factors, and clinical implications. J Am Coll Cardiol. 2016;68(19):2059-2069
8. Tay EL et al. A high -risk period for cerebrovascular events exists after transcatheter aortic valve implantation. JACC Cardiovasc Interv. 2011;4(12):1290-7
9. Makkar RR et al. Possible subclinical leaflet thrombosis in Bioprosthetic aortic Valves. N Engl J Med. 2015;373(21):2015-24.
10. Auffret V et al. Serial changes in cognitive function following transcatheter aortic valve replacement. J Am Coll Cardiol. 2016;68(20):2129-2141
11. Spaziano M et al. Imaging and functional testing to assess clinical and subclinical neurological events after transcatheter or surgical aortic valve replacement: a comprehensive review. J Am Coll Cardiol. 2014;64(18):1950-63

Aortic Regurgitation (AR)

Acute and chronic AR have different etiologies, pathophysiological consequences, natural histories, and management strategies. In general, AR occurs when the aortic valve does not close (or coapt) completely and blood flows back into the LV from the aorta during diastole. As shown in **Figure 1**, this results in a rapid descent of aortic diastolic pressure (AP tracing). Backflow from Aorta to LV → Increase in LVEDV → increased LV preload → increased SV and SBP. Increased SBP and decreased DBP as described above result in characteristic wide pulse pressure.

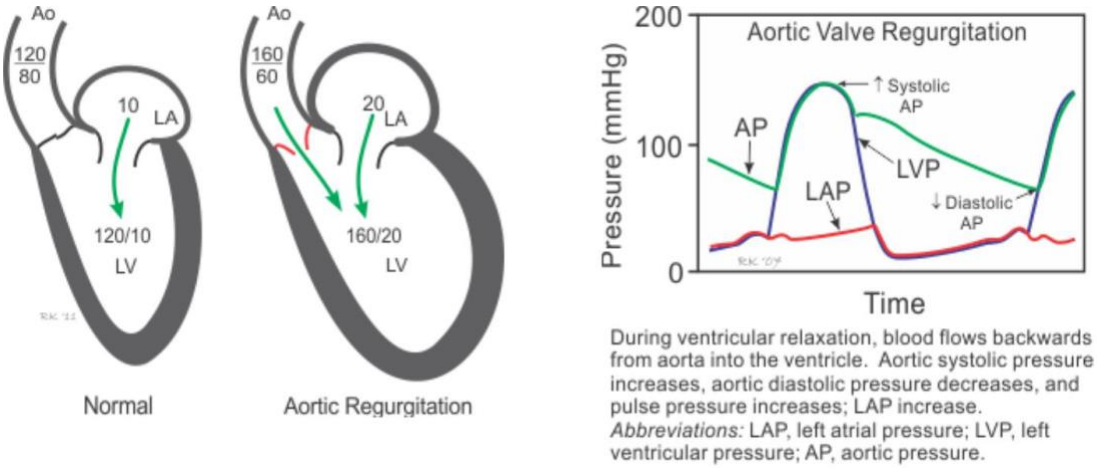


Figure 1. Aortic Regurgitation. *CVPhysiology.com.*

Acute AR:

Etiology and Epidemiology

Results from abnormalities of the valve, such as infective endocarditis, or cusp prolapse, or acute abnormalities of the aorta, primarily aortic dissection. Acute AR may also occur among patients with mechanical or bioprosthesis if there is prosthetic leaflet dysfunction.

Pathophysiology:

In the uncompensated heart with acute AR, an increase in LVEDV (without acute LV enlargement) results in a large increase in left-sided pressures, which leads to congestive heart failure and pulmonary edema. Marked and rapid volume overload pushes the LV to the edge of its Frank-Starling curve. The LV cannot acutely increase total stroke volume, resulting in a decline in forward stroke volume and cardiac output.

Acute AR may be an **emergency**; if a patient is symptomatic from acute AR, surgical consultation should be pursued.

Chronic AR:

Etiology/Epidemiology:

The most common causes of chronic AR in the United States and other developed countries are bicuspid aortic valve, thoracic aneurysms and calcific valve disease. Rheumatic heart disease is the leading cause in many developing countries. AR also arises from primary diseases causing dilation of the ascending aorta or sinuses of Valsalva (e.g. genetic syndromes such as Marfan's Syndrome, systemic rheumatic disorders such as ankylosing spondylitis, and infectious aortitis).

The 2018 AHA/ACC Adult Congenital Cardiology guidelines provide a Class IIa recommendation to screen first-degree relatives of individuals with bicuspid aortic valve for valvular disease (present in 10% of relatives) and aortopathy (present in 32% of relatives).[1]

Pathophysiology and Clinical Course

Chronic AR typically leads to progressive LV and LA dilation. The added volume produces an increased wall tension and, over time, spherical remodeling and eccentric ventricular hypertrophy. Ventricular compliance increases to accommodate high volumes. The combination of ventricular hypertrophy and increased preload raises the stroke volume, and cardiac output is initially maintained. In this way, patients with moderate-severe AR may remain asymptomatic for years.

Over time, however, the LV continues to dilate and the hypertrophy is unable to keep pace, which eventually leads to a decline in both LV contractility and ejection fraction (EF). Interstitial fibrosis increases, compliance declines, and LVEDP rises, and symptoms of congestion ensue. Bradycardia is poorly tolerated because slow HRs increase diastolic filling (and regurgitant volume) time, which reduces effective forward stroke volume.

Initial Clinical Evaluation

Physical exam:

- **Early decrescendo diastolic murmur at the LUSB or RUSB.** This murmur typically **increases** with sitting forward, expiration, or handgrip (increase in afterload). The murmur is louder with more severe AR, except if AR is acute or in its late-stage when LV filling pressure rises and aortic pressure drops.
- The **Austin Flint murmur,** a diastolic rumble at the apex, may also be audible if the AR jet is directed posteriorly and interferes with mitral inflow.
- An S3 is common and can be heard in patients with AR and a preserved EF (due to LV dilation that is part of the normal pathophysiologic response to AR).
- Pulses may be bounding, and the pulse pressure is widened. These and dozens of other eponymous signs become increasingly prominent as the AR becomes more severe.

Radiographic evaluation:

- TTE is indicated in patients with signs or symptoms of AR for accurate diagnosis of the cause of regurgitation; assessment of regurgitant severity, LV size and LV systolic function; and for determining timing of valve intervention. See **Figure 2** and **Table 1** below for echocardiographic/clinical grading criteria.

- If TTE images are sub-optimal in moderate/severe AR, or clinical and echocardiographic findings are discrepant, can **consider TEE or cardiac MRI** (less useful in acute setting), to distinguish between moderate and severe MR

  Note: In cases of acute AR when aortic dissection is suspected, the sensitivity and specificity of TTE for dissection is only around 60 to 80%. In these instances, TEE or CTA should be employed, as the sensitivities and specificities for diagnosing aortic dissection exceed 95% for these modalities.

- AR is quantified by measuring the jet width in the LVOT and vena contracta (the narrowest width of the regurgitant jet before the LVOT) on Doppler as well as the regurgitant orifice size and regurgitant volume. With severe AR, Doppler shows steep deceleration in the jet velocity due to elevated LV end-diastolic pressure and prolonged diastolic flow reversal in the descending aorta.

- LV systolic and diastolic diameters, EF, and aortic width on TTE are key parameters that influence decision for surgical intervention. Depressed ejection fraction and increased LVESV are associated with development of HF symptoms or death in asymptomatic patients.

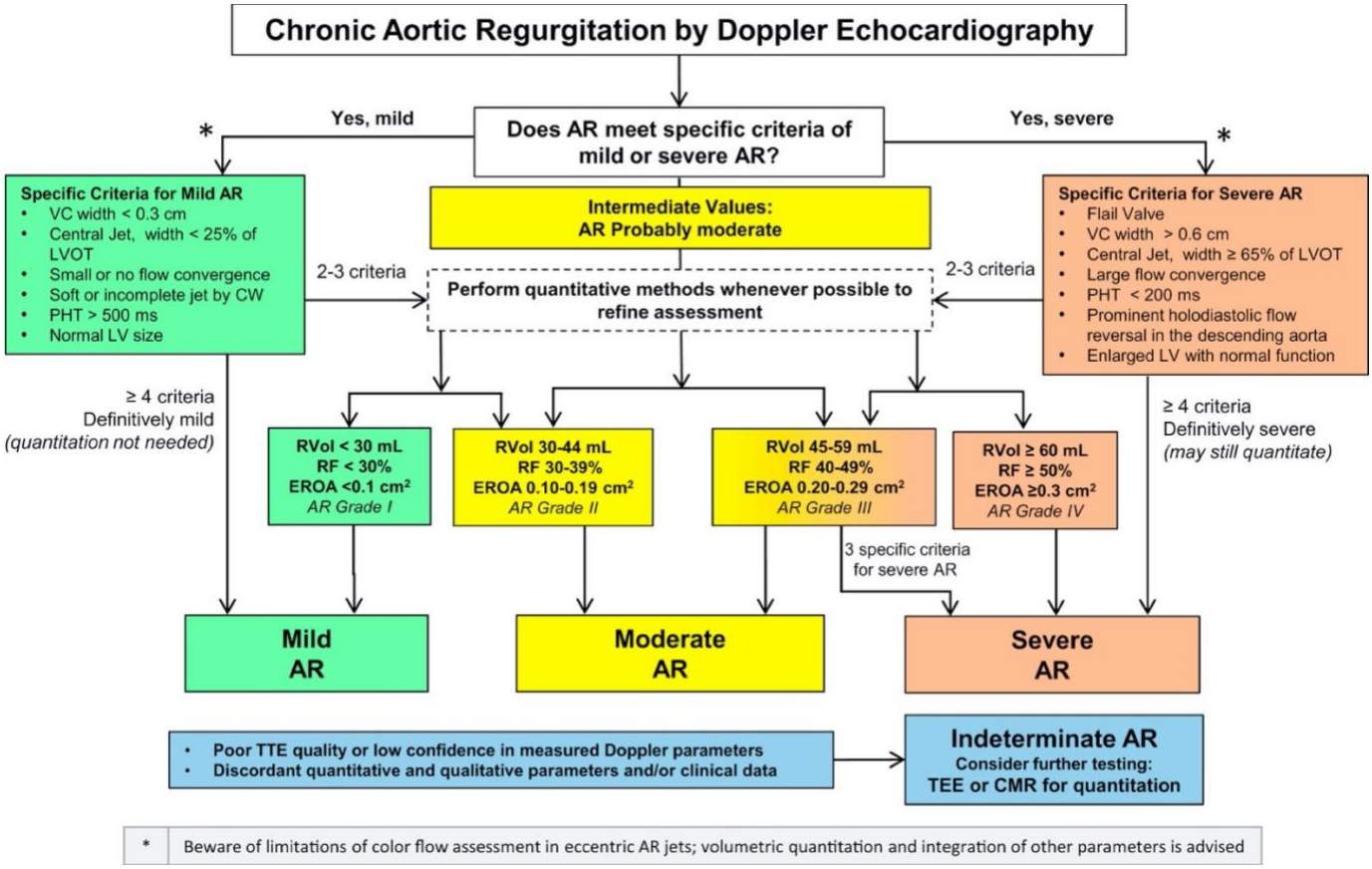


Figure 2. Echocardiographic assessment of aortic regurgitation severity. *Asecho.org.*

Table 1: 2020 ACC/AHA Guidelines for Staging Chronic AR[3]

	Progressive (stage B)	**Asymptomatic Severe (Stage C)**	**Symptomatic Severe (Stage D)**
Hemodynamics			
Jet width (% of LVOT)	Mild: <25% Moderate: 25-64%	Severe: ≥65%	Severe: ≥65%
Vena contracta (cm)	Mild: <0.3 cm Moderate: 0.3-0.6 cm	Severe: >0.6 cm	Severe: >0.6 cm
Regurgitant volume (ml/beat)	Mild: <30 ml Moderate: 30-59 ml	Severe: ≥60 ml	Severe: ≥60 ml
Regurgitant fraction (%)	Mild: <30% Moderate: 30-49%	Severe: ≥50%	Severe: ≥50%
Effective regurgitant orifice (cm^2)	Mild: <0.10 cm^2 Moderate: 0.10-0.29 cm^2	Severe: ≥0.3 cm^2	Severe: ≥0.3 cm^2
Diastolic aortic flow reversal	Sub-holosystolic	Holosystolic	Holosystolic
LV size/function	Normal LV volume or mild dilation. Normal LV systolic function	C1: LVEF ≥55%, mild-moderate LV dilation. C2: LVEF <55% or severe LV dilation (LVESD>50mm)	Moderate-to-severe LV dilation is present. Can occur with normal LVEF (≥55%), mild-moderate dysfunction (40-55%) or severe LV dysfunction (<40)

*****Note: **Stage A** refers to “at-risk” patients, such as patients with bicuspid aortic valve, diseases of the aortic sinus or ascending aorta, history of rheumatic fever, or infective endocarditis.

Surveillance:
Repeat TTE should be performed to re-evaluate asymptomatic patients with AR, with recommended frequency determined by the severity of regurgitation (Severe: every 6-12 months, Moderate: every 1-2 years, Mild: every 3-5 years).

Management
Medical Management
Acute or decompensated AR: The management of acute severe AR (most often resulting from infectious endocarditis or aortic dissection) consists of hemodynamic temporization and urgent surgical evaluation. Propensity-matched cohort studies among patients with infective endocarditis have demonstrated a 6% absolute risk reduction with early versus delayed surgery.[2]

Medical therapy:
- IV afterload reduction with agents like nitroprusside. Avoid vasoconstrictors which may increase diastolic regurgitant flow
- Inotropic support with dobutamine/milrinone as needed
- Chronotropic support with overdrive pacing or isoproterenol to reduce diastolic regurgitation time as needed.
- Beta blockers are generally avoided in severe AR (blocks compensatory tachycardia, increasing diastolic regurgitation time), except in the case of acute aortic dissection where it is first line for impulse control therapy
- Diuretics as needed to reduce LV filling pressures
- Consider PA line placement for guidance of above therapies

Mechanical Circulatory Support
- Intra-aortic balloon pumps are **contraindicated** in severe AR: inflate during diastole → increase diastolic regurgitant flow dramatically
- VA ECMO is contraindicated in patients with severe aortic regurgitation
- LVAD implantation can worsen AR. Significant AR can lead to ineffective LVAD output and end-organ malperfusion.

Chronic compensated AR:
- In asymptomatic patients with chronic AR (stages B and C), treatment of hypertension to maintain SBP <140 mm Hg is recommended
- Guidelines recommend the use of ACE inhibitors/ARBs in patients with severe AR who have symptoms and/or LV dysfunction and are not candidates for surgical intervention. RCTs have not shown conclusively that these drugs alter the natural history of asymptomatic patients with chronic asymptomatic AR and normal LV systolic function, but cohort studies support their use in patients with systolic impairment.

Valvular intervention
- Proceed to AVR if patient is symptomatic, LVEF <50%, LV end-systolic dimension >50 mm, and/or if concomitant CT surgical procedure is being planned (i.e. CABG or other valve). See Figure 3.
- Outcomes are optimal when surgery is performed before LVEF decreases below 55%.
- In asymptomatic patients with LV systolic dysfunction, postoperative outcomes are better if AVR is performed before onset of symptoms.

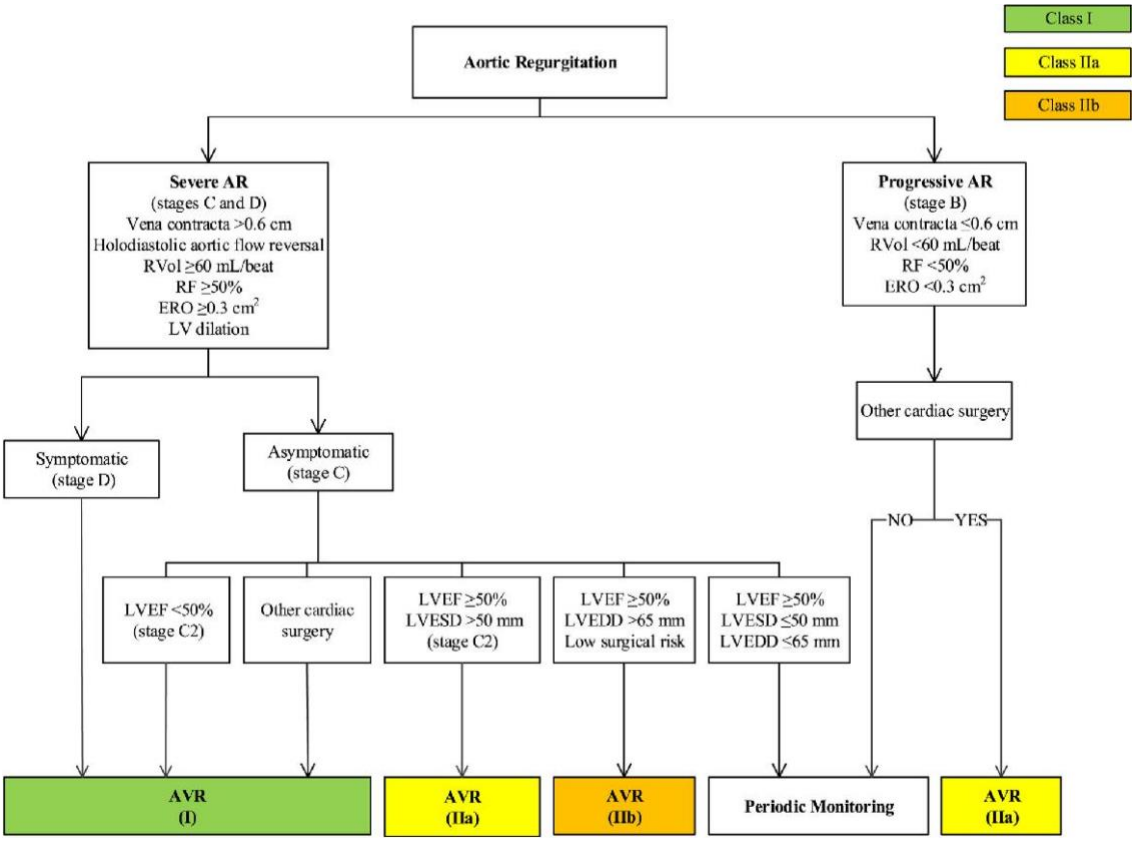


Figure 3. Timing of Valvular Intervention. *2014 ACC/AHA Guidelines 2014.*

Additional Notes:

- Once AR has been diagnosed, follow up evaluations should focus on the identification of symptoms. Symptomatic AR is an indication for surgical intervention, and intervening as early as possible—before LV systolic failure ensues or worsens—is paramount. Without AVR, these patients have a very high mortality rate (25% for NYHA class III/IV, 6% for NYHA Class II), and post-operative survival is significantly higher in patients who are still NYHA I/II at time of surgery compared with NYHA class III/IV (10 year survival of 80% vs 45%).[4]
- Even in symptomatic patients with severely depressed systolic function, surgery is recommended over medical therapy. The sooner AVR is performed after depressed EF is noted, the more systolic recovery occurs.

References:

1. Stout KK et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease. J am Coll Cardiol. 2019;73(12):1494-1563
2. Lalani T et al. Analysis of the impact of early surgery on in-hospital mortality of native valve endocarditis: use of propensity score and instrumental variable methods to adjust for treatment-selection bias. Circulation. 2010;121(8):1005-13.
3. 2014 AHA/ACC guideline for the management of patients with valvular heart disease. J Am Coll Cardiol. 2014 Jun 10;63(22):2438-88
4. Klodas E et al. Optimizing timing of surgical correction in patients with severe aortic regurgitation: role of symptoms. J Am Coll Cardiol. 1997;30(3):746-52

Mitral Regurgitation (MR)

Etiology and Epidemiology

Acute.
Etiologies: Acute ischemia (most often inferior STEMI) with papillary muscle rupture/dysfunction, infective endocarditis, spontaneous chordal rupture in myxomatous mitral valve disease

Chronic.
(1) Primary (degenerative). Valvular incompetence via pathology of a component of the **valve itself (leaflets/chordae tendinae/papillary muscles/annulus)**.

- **Most common cause** in United States is MVP and ischemic heart disease. Additional etiologies: infective endocarditis, rheumatic heart disease, collagen vascular disease, annular calcification
- Young patients**: myxomatous degeneration**
- Elderly patients: **fibroelastic degeneration** of valve

(2) Secondary (functional). Valve is normal but becomes displaced via papillary muscle displacement (usually from dilated ventricle and severe LV dysfunction). Annulus dilates, leaflet becomes tethered, and valve leaflets cannot coapt.

Pathophysiology and Clinical Course

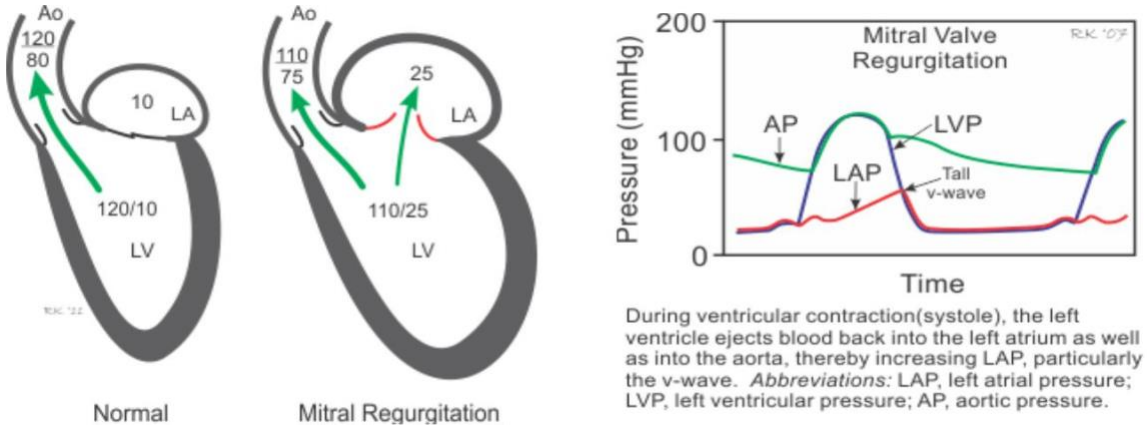


Figure 1. Mitral regurgitation. *CVphysiology.com.*

Acute Mitral Regurgitation.

- Acute MR and sudden volume overload cannot be compensated by LV → risk of pulmonary edema, reduced SV and CO, cardiogenic shock

Chronic Primary Mitral Regurgitation.

- ↑ LA volume and pressure → ↑ pulmonary circulation pressures and ↑ LVEDV → enlarged LV.
  - Increased LV size leads to risk of atrial fibrillation and worsens MR by dilating mitral annulus/regurgitant orifice.
  - LV undergoes eccentric hypertrophy with compensatory dilation (volume overload pattern). Initially maintains CO, but decompensates and leads to left, then right sided heart failure and ↑risk sudden death.

In those who are symptomatic, exertional dyspnea, fatigue, and atrial fibrillation are the most common manifestations. Severe MR results in poor clinical outcomes (survival rates 33% at 8 years without MVR, mortality 5% per year). Most deaths are due to heart failure. There is a substantial rate of sudden death, highlighting the importance of ventricular arrhythmias.

Evaluation: 1. Distinguish between acute and chronic. 2. Identify etiology. 3. TTE to confirm and grade severity.

Acute.
History: **New onset** dyspnea, PND, orthopnea, edema. Exam: **New apical holosystolic murmur radiating to left axilla**. Rales, edema, JVD, cardiogenic shock.

Chronic.
History: **Progressive exertional dyspnea**, exercise intolerance.
Exam: **Apical holosystolic murmur radiating to left axilla** *(half patients with chronic secondary MR lack audible murmur, especially if low systolic LA-LV pressure gradient i.e. ↑LA pressure, ↓systemic arterial pressure)* decreased with maneuvers which decrease venous return (Valsalva). Specific findings per etiology: mid-systolic click (MVP), S3 gallop, lateral PMI (LV dilatation), rales (pulmonary edema). AF highly associated with chronic MR with LA dilatation.

- Other possible findings: Early diastolic rumble, left sided S4, soft S1 and widely split S2. Sharp and high volume carotid upstroke when severe. Cardiac impulse brisk, hyperdynamic, laterally displaced.

Radiographic findings other than TTE:

- EKG: Acute MR usually no specific findings. Chronic MR: Large LA, large LV. P-mitrale often associated mostly with chronic MR
- CXR: Large LA, large LV, pulmonary edema occasionally unilateral (RUL common from posteriorly directed regurgitant jet)
- RHC: large V waves suggestive (Figure 1)

TTE is most common modality for diagnosis of MR. Echo criteria are used to grade MR (Tables below). ACC/AHA guidelines support the use of TTE for initial evaluation (EF, LV and LA sizes, and PA pressure). Consider TEE as well before surgical intervention if TTE not sufficient for mechanism of MR and feasibility of repair (although sedation during TEE can reduce degree of MR via vasodilation and afterload reduction).

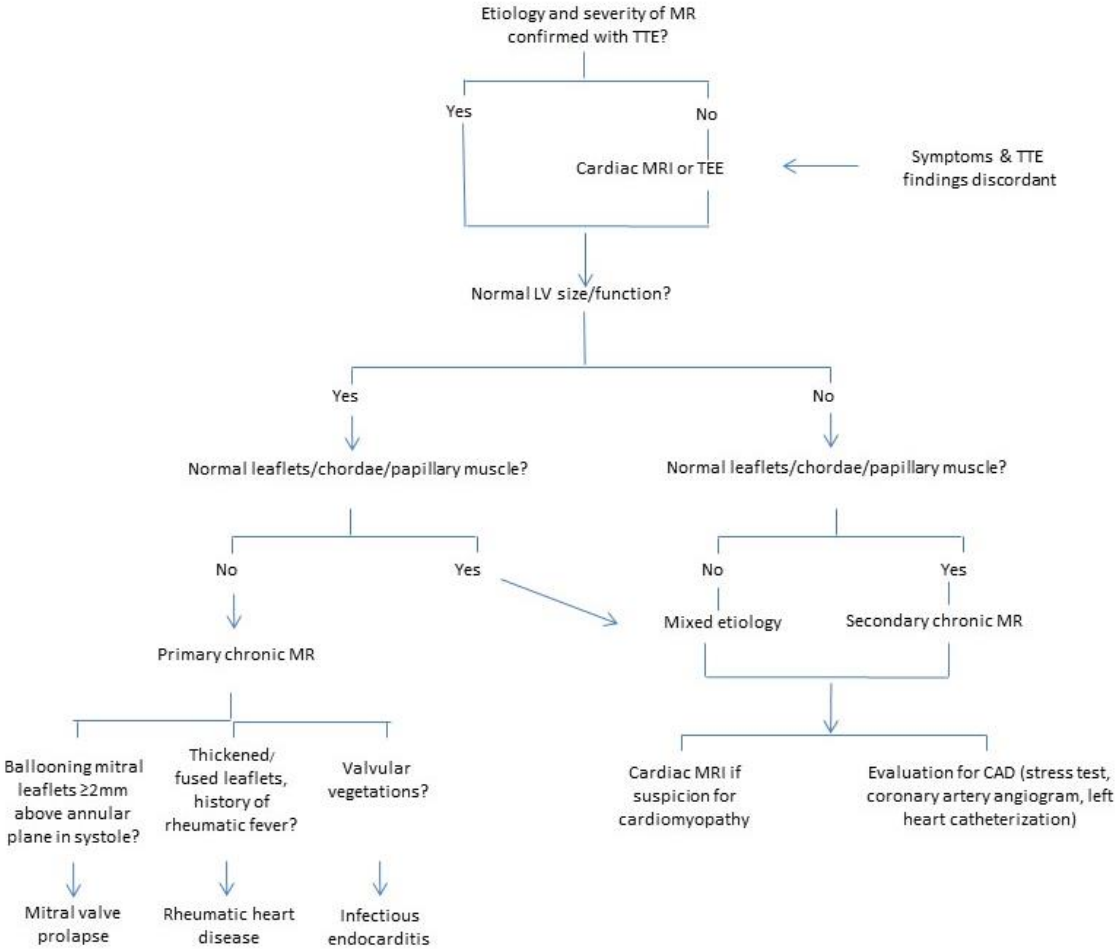


Figure 2. Algorithm for determining etiology of MR.

The criteria for grading MR are shown in Table 1-2. The clinical progression of the disease is separated into stages A-D. Stage A is mild MR. Stage B is moderate MR. Stage C-D are severe MR. For severe, chronic MR, only one echocardiographic criteria must be met.

Table 1: 2020 ACC/AHA guidelines for Stages of Chronic Primary MR

Stage	*A*	*B*	*C*	*D*
Definition	At risk of MR	`Progressive MR	Asymptomatic severe MR	Symptomatic Severe MR
Valve Anatomy	- Mild MVP - Normal coaptation - Mild valve thickening and leaflet restriction	- Mod-severe MVP - Normal coaptation - Rheumatic valve changes with leaflet restriction and loss of central coaptation - Prior IE	- Severe MVP - Loss of coaptation or flail leaflet - Rheumatic valve changes with leaflet restriction and loss of central coaptation - Prior IE - Thickening of leaflets with radiation heart disease	
Valve Hemodynamics *Doppler MR jet area*	- No or small central jet area <20% LA	- Central jet MR 20-40% LA or late systolic eccentric jet MR	- Central jet MR >40% LA or holosystolic eccentric jet MR	
Doppler vena contracta	<0.3cm	<0.7cm	≥0.7cm	
Regurgitant volume (mL/beat)		<60mL	≥60mL	
Regurgitant fraction <50%		<50%	≥50%	
ERO		<0.40cm^2	≥0.40cm^2	
Angiographic grade		1+ to 2+	3+ to 4+	
Hemodynamic Consequences	None	Mild LA enlargement No LV enlargement Normal pulmonary pressure	Mod-severe LA enlargement LV enlargement Pulmonary HTN at rest or with exercise C1: LVEF>60% and LVESD<40mm C2: LVEF≤60% and/or LVESD ≥40mm	Mod-severe LA enlargement LV enlargement Pulmonary HTN at rest
Symptoms	None	None	None	Decreased exercise tolerance Exertional dyspnea

Not all criteria for each valve hemodynamic criteria need to be present in each patient. Parameters should be integrated with other clinical evidence. ERO, effective regurgitant orifice; IE, infective endocarditis; LA, left atrium; LV, left ventricular; LVESD, left ventricular end-systolic dimension; MVP, mitral valve prolapse.

Table 2: 2020 ACC/AHA guidelines for Stages of Chronic Secondary MR

Stage	*A*	*B*	*C*	*D*
Definition	At risk of MR	Progressive MR	Asymptomatic severe MR	Symptomatic Severe MR
Valve Anatomy	Normal valve leaflets, chords, and annulus in a patient with CAD or cardiomyopathy	- Regional wall motion abnormalities with mild tethering of mitral leaflet Annular dilation with mild loss of central coaptation of the mitral leaflets	- Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet Annular dilation with severe loss of central coaptation of the mitral leaflets	
Valve Hemodynamics *Doppler MR jet area*	- No or small central jet area <20% LA			
Doppler vena contracta	<0.3cm			
Regurgitant volume (mL/beat)		<60mL	≥60mL	
Regurgitant fraction <50%		<50%	≥50%	
ERO		<0.40cm^2	≥0.40cm^2	
Associated Cardiac Findings	Normal or mildly dilated LV size with fixed (infarction) or inducible (ischemia) regional wall motion abnormalities Primary myocardial disease with LV dilation and systolic dysfunction	Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction attributable to primary myocardial disease	Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction attributable to primary myocardial disease	
Symptoms	Symptoms attributable to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy		HF symptoms attributable to MR persist even after revascularization and optimization of medical therapy Decreased exercise tolerance Exertional dyspnea	

Not all criteria for each valve hemodynamic criteria need to be present in each patient. Parameters should be integrated with other clinical evidence. ERO, effective regurgitant orifice; IE, infective endocarditis; LA, left atrium; LV, left ventricular; LVESD, left ventricular end-systolic dimension; MVP, mitral valve prolapse.

Management

Acute MR:

Surgical repair > transcatheter repair. Consider early revascularization if ischemia.

> *Additional notes: This usually requires urgent and early surgical repair. Worse prognosis than chronic MR. Early revascularization (if ischemic) may arrest local maladaptive LV modeling, restore valve competence, and obviate the need for surgical repair. Surgical repair generally preferred over transcatheter repair.*

Medical management to stabilize for surgery. Reduce afterload, maintain CO and diminish pulmonary congestion with IV nitroprusside, dobutamine, or intra-aortic balloon pump.

Chronic primary MR: Mainstay is surgery.

The decision to proceed depends on symptoms, LVEF, LVESD. Recommendations:

- Mitral valve intervention recommended irrespective of LV systolic function: symptomatic patients with severe primary MR
- Mitral valve surgery recommended: asymptomatic patients with severe primary MR and LVEF <60%, LVESD >40mm
- Mitral valve repair is reasonable: Asymptomatic patients with severe primary MR and LVEF >60 and LVESD <40mm, when performed at a primary or comprehensive valve center and has a high likelihood of a successful and durable repair (chance of no residual MR >95%, mortality <1%)
- Mitral valve surgery can be considered : asymptomatic patients with severe primary MR and LVED>60 and LVESD <40mm but with progressive increase in LV size of decrease in EF on >3 serial imaging studies (do not need to consider likelihood of a successful and durable repair)
- Mitral valve repair can be considered: symptomatic patients with severe primary MR attributable to rheumatic valve disease, at a comprehensive Valve Center if durable and successful repair is likely.
- Transcatheter edge-to-edge repair is reasonable: severely symptomatic patients (NYHA class III or IV) with primary severe MR and high/prohibitive surgical risk, if anatomy favorable and life expectancy at least 1 year.

Additional notes: If surgery will proceed, the next determination is mitral valve repair vs replacement followed by the decision of mechanical vs bioprosthetic valve. Among patients with severe symptomatic MR, mortality is as high as 8% per year, and the mainstay of therapy is surgery.

***Mitral valve repair is preferred** over replacement if valve morphology is amenable, as valve repair is associated with superior post-operative survival and ventricular function. Involvement of the anterior leaflet (or both leaflets) may preclude repair and require replacement. Repair further eliminates the risks and pitfalls associated with prosthetic valves, including prosthesis degeneration. Around half of patients with bioprosthetic MVR will need another replacement within 15 years.*
For those who are symptomatic despite GDMT and have prohibitive surgical risk, transcatheter mitral valve repair with MitraClip can be considered

Medical management:

- Treat patients with symptomatic chronic primary MR stage D and LVEF<60% with GDMT as bridge to surgery or if prohibitive surgical risk.
- Treat concomitant hypertension per standard therapy.
- Patients with asymptomatic chronic primary MR stages B and C with normal LV systolic function do not receive medical treatment.

Chronic secondary MR: In contrast to primary MR, the utility of surgical intervention in chronic secondary MR is generally low due to the pathophysiology of this disease. If concomitant HFrEF, treat with GDMT.

There are no Class I indications for MV surgery for chronic secondary MR. Class II recommendations:

- MV surgery is reasonable: undergoing CABG concurrently for myocardial ischemia
- MV surgery can be considered: preserved LV systolic function (LVEF >50) with severe persistent symptoms (NYHA class III, IV) despite therapy for HF and comorbidities.
- MV surgery can be considered: reduced LV systolic function (LVEF <50) with severe persistent symptoms (NYHA class III, IV) on optimal GDMT
- Cardiac resynchronization therapy (CRT) can also be helpful in reducing the severity of functional MR if otherwise clinically indicated.[1]
- If surgery will proceed, mitral valve replacement is preferred over repair.

There are no Class I indications for TEER for chronic secondary MR. Class II recommendations:

- In patients with chronic severe secondary MR related to LV dysfunction LVEF<50% with NYHA class II, III, or IV symptoms while on optimal GDMT, TEER is reasonable with appropriate anatomy on TEE and LVEF 20-50%, LVESD <70, PASP <70mmHg.

Monitoring:
Repeat TTE if there are changes in symptoms.

In the absence of clinical change, repeat TTE every 6–12 months for patients with severe MR for evaluation of EF (more frequently if evidence of LV dilatation), every 1-2 years for moderate MR, every 3-5 years for mild MR.

Guidelines for anticoagulation after MVR (institutional preferences may vary, check with fellow/attending). Note that if reversal of anticoagulation is urgently needed, FFP can be used (Class II) and is preferred over Vitamin K since it is thought to reduce the incidence of thrombotic complications (though no good data).

- Bioprosthetic MVR: 81 mg ASA, 3 month of Coumadin for INR 2–3 after surgery (lifetime if rheumatic MR or if EF<30–35, hypercoag, hx clot, AFib)
- Mechanical MVR: 81 mg ASA, INR 2.5–3.5 for life with IV heparin when INR <2.5

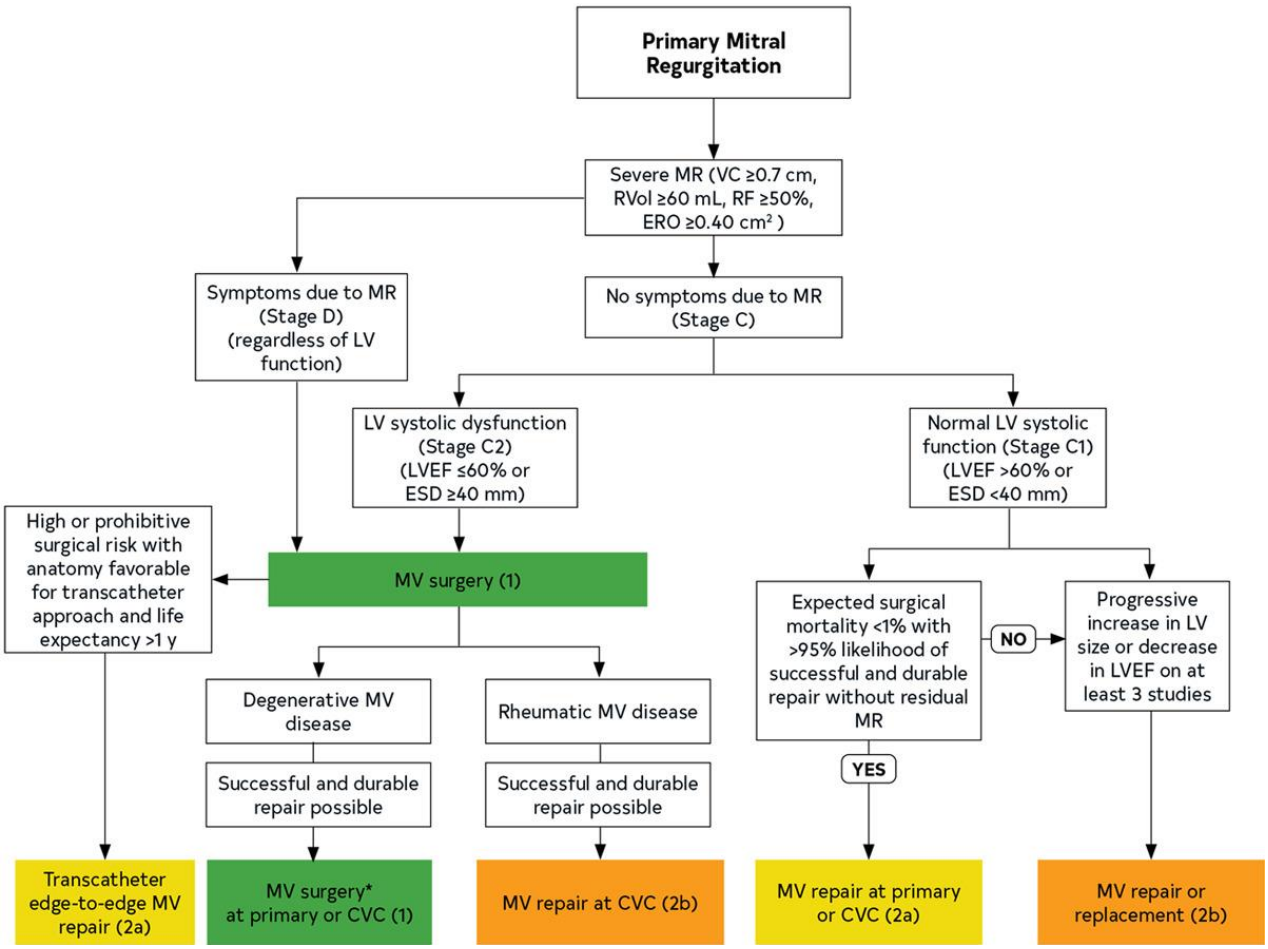


Figure 3. Indications for Intervention for Primary MR. *ACC/AHA 2020*[2]

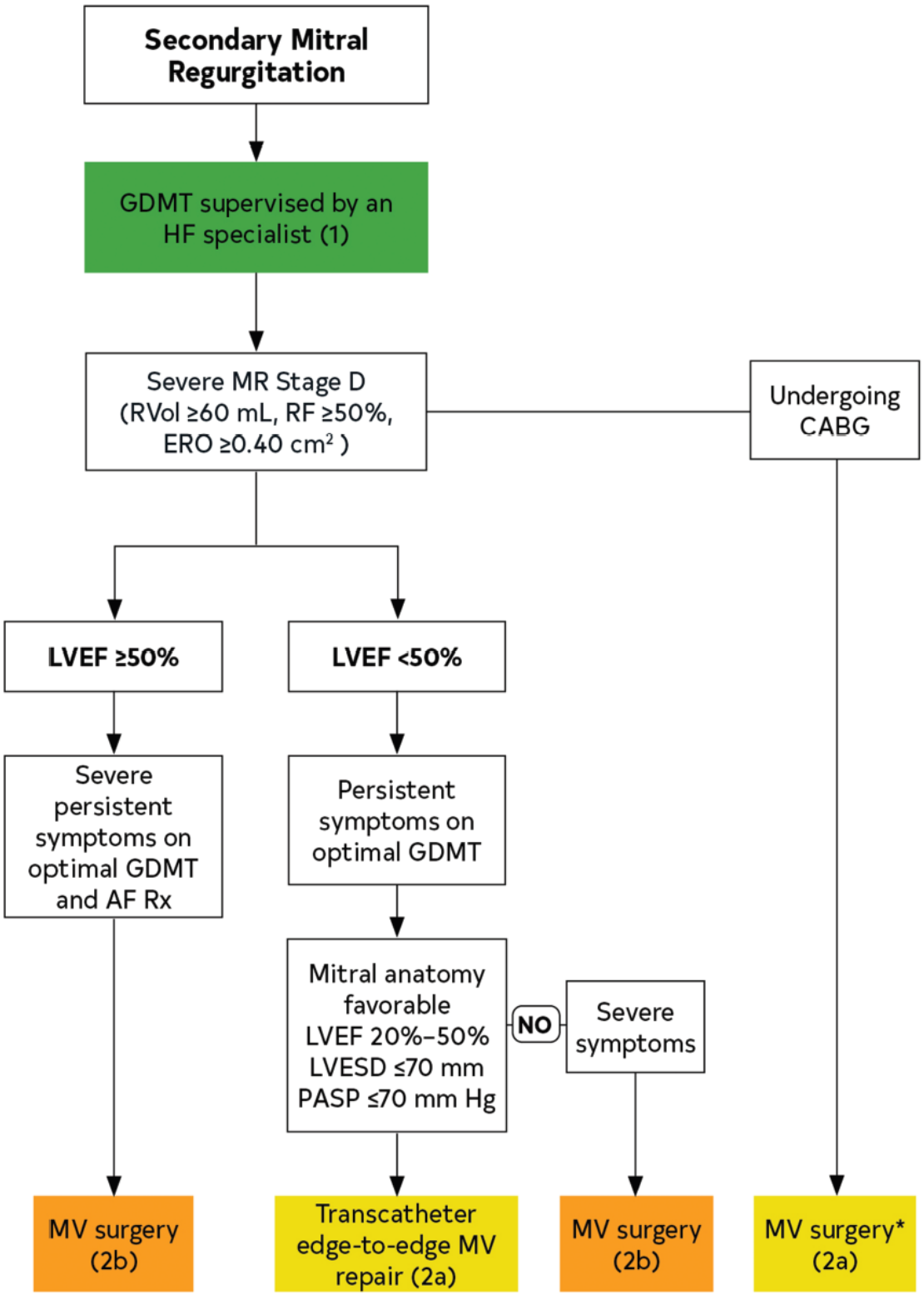


Figure 4. Indications for Intervention for secondary MR. *ACC/AHA 2020*[2]

References:

1. van Bommel RJ et al. Cardiac resynchronization therapy as a therapeutic option in patients with moderate-severe functional mitral regurgitation and high operative risk. Circulation. 2011;124(8):912-9.
2. 2020 AHA/ACC guideline for the management of patients with valvular heart disease. J Am Coll Cardiol. 2014 Jun 10;63(22):2438

Mitral Stenosis (MS)

Etiology and Epidemiology

Etiologies: **rheumatic fever**, then **senile calcific MS**. Other rare cause is congenital (parachute, supramitral ring, part of Shone's complex)

- Rheumatic → progressive, thickening of leaflet edges, fusion of commissures, chordal shortening and fusion. Latent phase between initial illness and valve stenosis.
- Senile calcific → benign calcification of annulus extends into leaflets → narrowing of annulus and rigidity of leaflets without commissural fusion. Can also be caused by radiation induced valve disease, often in survivors of Hodgkin's lymphoma.

Pathophysiology and Clinical Course

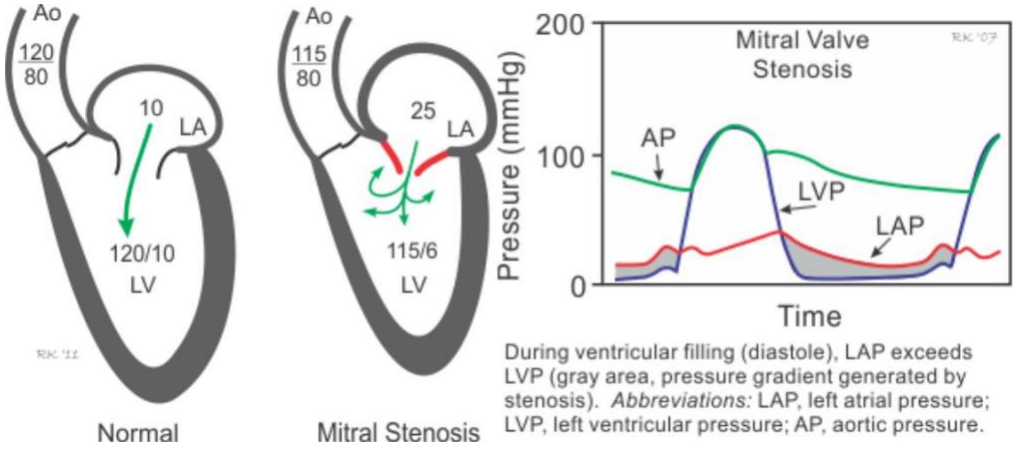


Figure 1. Mitral Stenosis. *CVPhysiology.com.*

- ↓LA flow to LV → ↑LA pressure, ↑pressure in pulmonary vasculature, ↑right sided pressures.
- Nonspecific presentation: exertional dyspnea, poorly tolerated AF from loss of atrial kick or rapid heart rate, unexplained cardio embolism, hemoptysis from increased pulmonary congestion, hoarseness from LA compression of recurrent laryngeal nerve (Ortner's Syndrome). Clinical history of childhood rheumatic fever or characteristic cardiac exam.
- Generally diagnosed echocardiographically
- If untreated: progressive pulmonary edema → pulmonary hypertension and right heart failure (60% of cases) →death. Mortality can also result from systemic thromboembolic events in the context of atrial fibrillation.

Evaluation

TTE is indicated to 1. Diagnose MS. 2. Determine etiology. 3. Grade severity. 4. Typify valve morphology to determine suitability for percutaneous mitral balloon commissurotomy (PMBC)

- TTE can show:
  - Characteristic diastolic doming of mitral valve (seen on parasternal long-axis)
  - Commissural fusion and planimetry of mitral orifice (seen on short-axis, better done with 3D TTE)
  - Doppler hemodynamics (Seen on apical 4-chamber view)
  - Mitral valve morphology and PMBC suitability scored via Wilkins/MGH score on a 16-point scale (>8 less favorable)
- TEE is alternative with technically limited transthoracic windows, is necessary to exclude LAA thrombus prior to PMBC and to evaluate presence of concomitant MR

Exam:
Loud S1 leading to softer S1 as leaflets become more calcified, opening snap heard best at base, low pitched diastolic rumble (most prominent at apex in left lateral decubitus during held expiration using stethoscope bell),

The criteria for grading MS are shown in Table 1. The clinical progression of the disease is separated into stages A-D.
Table 1. 2020 ACC/AHA Guidelines for Staging MS

Stage	*A*	*B*	*C*	*D*
Definition	At risk of MS	`Progressive MS	Asymptomatic severe MS	Symptomatic Severe MS
Valve Anatomy		Rheumatic valve changes with commissural fusion and diastolic doming of mitral valve leaflets		
Visual appearance	Mild valve doming during diastole			
Mitral Valve Area (planimetered)		>1.5cm^2	≤1.5cm^2	
Valve Hemodynamics				
	Normal transmitral flow velocity	Increased transmitral flow velocities		
Mitral Valve Area (by continuity equation)		>1.5cm^2	≤1.5cm^2	
Diastolic pressure half time		<150ms	≥150ms	
Hemodynamic Consequences				
LA enlargement	None	Mild to moderate	Severe	
Pulmonary artery systolic pressure		Normal	>50 mmHg	
Symptoms		None	Decreased exercise tolerance Exertional dyspnea	

The transmitral mean pressure gradient should be obtained to further determine hemodynamic effect of MS and is usually >5-10mm Hg in severe MS; However, due to the variability of the gradient with HR and output, it is not included in criteria for severity. LA left atrial; MS, mitral stenosis; PASP, pulmonary artery systolic pressure

Follow up and Surveillance

Repeat TTE should be performed to re-evaluate asymptomatic patients with MS. For Very Severe: every year, Severe: every 1-2 years, Progressive MS: every 3-5 years. The mean rate of progressive valve narrowing is ~0.1cm^2 per year with appreciable variability.

Management

Anticoagulate in rheumatic MS with AF and prior embolic events. It has been shown to reduce incidence of arterial embolization. There is evidence for VKA, but not for NOACs (patients with MS were excluded from AF trials).

If rheumatic MS and AF with RVR, or with symptomatic resting/exertional sinus tachycardia, use a beta blocker.

> *Additional notes: Negative dromotropes (e.g. beta blockers) can be beneficial in patients with rheumatic MS and either AF with RVR or with symptomatic resting or exertional sinus tachycardia. Studies of beta blockers and ivabradine demonstrated only benefit in younger patients without chronotropic incompetence; thus although there is theoretical benefit in reducing HR and prolonging diastolic filling (thereby preventing a rise in mean mitral gradient and increased LA pressures), this is balanced by limitation of stroke volume and chronotropic incompetence. Rheumatic disease itself can lead to fibrosis of conduction tracts and predispose to hard to control AF. Beta blockade is used in pregnant pts with MS to blunt the physiologic tachycardia of pregnancy and prolong diastole, prevent pulmonary edema.*

Diuretics are a mainstay of medical management to keep LA pressures down and manage pulmonary edema prior to intervention.

PMBC or open/closed commissurotomy are mainstay of therapy over medical management. Mitral valve replacement is an option only if no other options with severe limiting symptoms.

> *Additional notes: PMBC involves puncturing the septum during cardiac catheterization to access the stenotic mitral valve via RA to LA. A balloon is then inflated to force open the valve a separate the fused commissures; this is also what occurs during surgical commissurotomy. Other approaches with expanding roles in MS include transcatheter mitral valve replacement (TMVR) and mitral valve bypass. IN TMVR, for patients who cannot receive PMBC or surgery, an expandable transcatheter valve is inserted into the MV leaving the native MV tissue in place. In MV bypass a conduit is sewed from the LA to the LV apex and a prosthetic valve is incorporated into the conduit, avoiding direct manipulation of the mitral annulus.*

Recommendations:

- PMBC is recommended: patients with NYHA class II, III, IV, and severe rheumatic MS and favorable valve morphology with less than 2+ MR in the absence of LA thrombus, if at a Comprehensive Valve Center.
- Mitral valve surgery is indicated: patients with NYHA III or IV with severe rheumatic MS who are not candidates for PMBC, have failed a previous PMBC, require other cardiac procedures, or do not have access to PMBC.
- PMBC is reasonable: asymptomatic patients with severe rheumatic MS and favorable valve morphology with less than 2+MR in the absence of LA thrombus with elevated PASP>50mmHg, if at a comprehensive Valve Center
- PMBC may be considered: asymptomatic patients with severe rheumatic MS and favorable valve morphology with less than 2+MR in the absence of LA thrombus who have new onset of AF, if at a Comprehensive Valve Center.
- PMBC may be considered: NYHA II, III, IV with rheumatic MS, mitral valve area >1.5, if evidence of hemodynamically significant rheumatic MS with PAWP >25 or mean mitral valve gradient >15 during exercise, if at a Comprehensive Valve Center
- PMBC may be considered: NYHA III, IV with severe rheumatic MS with suboptimal anatomy and are not candidates for surgery, if at a Comprehensive Valve Center.

Calcific MS (or mitral annular calcification) is increasingly frequent in USA, but is usually high risk for any intervention given extensive calcification, advanced age, and comorbidities. Intervention only in highly symptomatic (NYHA III or IV) with severe MS (mitral valve area <1.5) attributable to extensive mitral annular calcification, with discussion of procedural risk and patient preferences and values. PMBC is not often performed here; feasibility studies show that TMVR may have a role. Nonrheumatic MS can also occur after radiation therapy or after a mitral valve repair with a small annuloplasty ring.

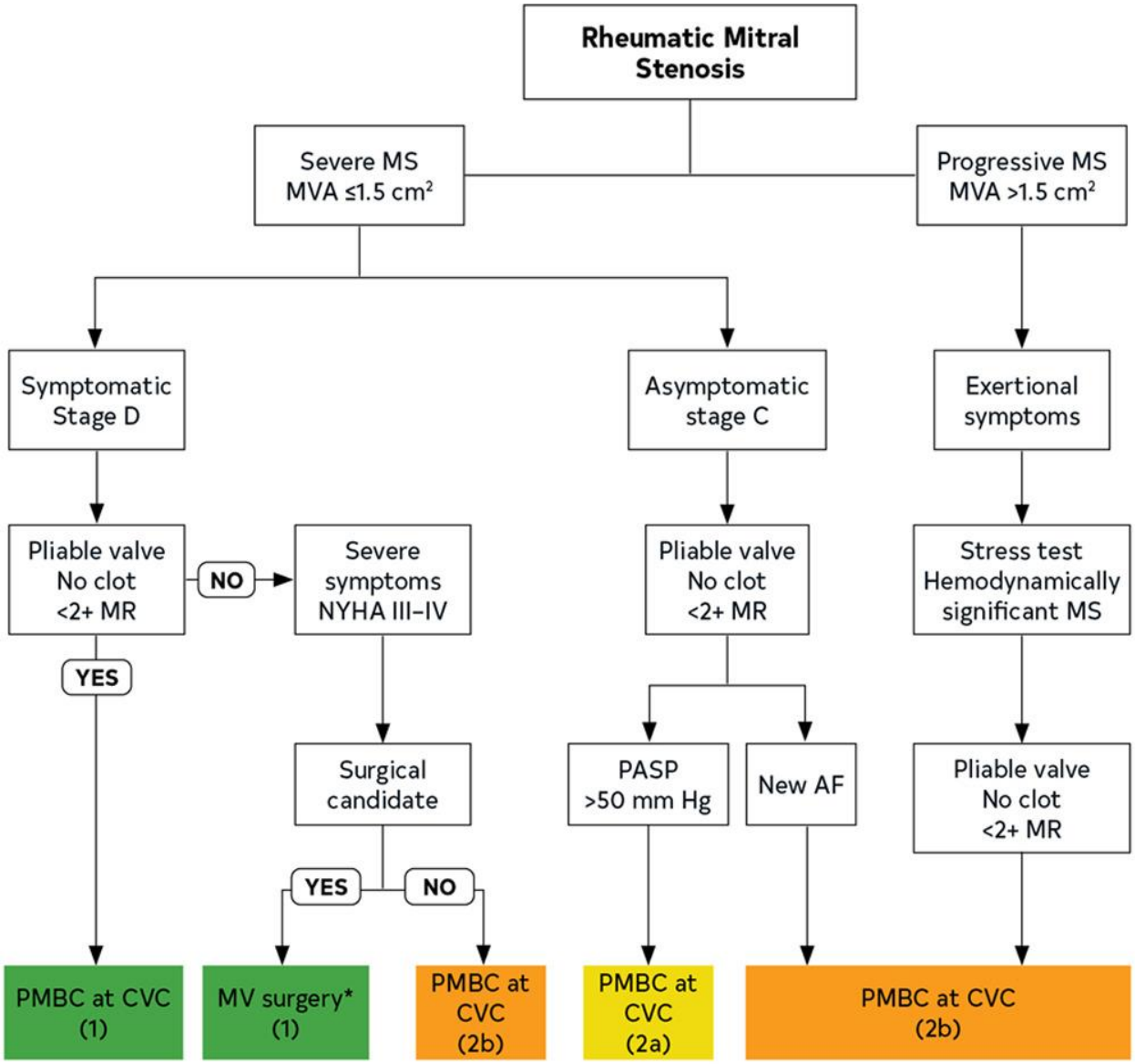


Figure 2. Indications for Intervention for MS. *ACC/AHA 2020*

Tricuspid Regurgitation (TR)

Etiology and Epidemiology
Some degree of TR is present in 70% of normal adults. TTE is indicated to determine etiology of TR (primary or secondary) and consequence on RV. Catheterization is of clinical value if TTE and clinical presentation are insufficient.

- (1) Primary.
    - Rheumatic disease, infective endocarditis, marantic endocarditis (SLE, RA), congenital (Ebstein's), myxomatous changes, blunt chest/deceleration trauma, carcinoid, drugs (fenfluramine/phentermine/pergolide), radiation, iatrogenic (leads, biopsies), ischemic heart disease causing papillary dysfunction or rupture, CTD (e.g. Marfan's)
    - In younger patients is mostly congenital, Ebstein's most common. Less common is trauma, IE, IVDU, and small ASD injuring valve through a jet.
- (2) Secondary. Most common form. TR with apparently anatomically normal leaflets/chords
    - Tricuspid annular dilation and leaflet tethering after RV remodeling from pressure or volume overload in pulmonary HTN or dilated cardiomyopathies. Also annular dilation associated with AF, and RV volume overload from shunts or high output states.
    - Disorders which induce RV dilatation and pulmHTN: left-sided HF, mitral stenosis/regurgitation, any primary pulmonary disease (e.g. PE), left-to-right shunt (ASD, VSD), Eisenmenger's syndrome, pulmonic valve stenosis, hyperthyroidism

Pathophysiology and Clinical Course
- Similar to MR

Evaluation
TTE is indicated to 1. establish diagnosis. 2. characterize severity. 3. measure velocity of TR for estimation of systolic RV to RA gradient 4. identify mechanism responsible for TR.

- TTE can show:
    - RV or RA dilation and RV function, tricuspid annulus dilation, paradoxical interventricular septal movement
    - Degree of pulmonary hypertension via estimation of RV to RA systolic gradient from TR jet peak velocity using modified Bernoulli equation
    - Doppler color flow using vena contracta method

Exam:
Clinical findings can be absent in TR and when present are often related to the underlying cause of TR, or its sequela, right-sided heart failure. In severe TR there may be a sensation of pulsation in the neck.

- Right-sided HF: painful hepatosplenomegaly, ascites, peripheral edema. When severe, cachexia, cyanosis, sometimes jaundice.
- Jugular veins: distended and prominent veins, distinct "c-v" wave from systolic regurgitation, pulsatile jugular vein (which can be confused with carotid arterial pulse), Kussmaul's sign (JVD more prominent with inspiration), systolic thrill felt over jugular vein when severe.
- Other findings: dynamic RV heave, dullness and prominent pulsation over left second intercostal space, peripheral edema, pleural effusions (if secondary to left-sided problem), hepatomegaly with possible thrill (transmission of systolic murmur)
- Auscultation: Holosystolic murmur best heard at left mid sternal border or subxiphoid area. No radiation and generally no palpable thrill. Murmur is soft/absent when TR is severe. Increases with inspiration/leg raise/exercise/hepatic compression. Standing decreases intensity of murmur. S3 often heard if RV very dilated; S4 possible if significant RV hypertrophy.

Table 1. 2020 ACC/AHA Guidelines for Staging Tricuspid Regurgitation

Stage	*B*	*C*	*D*
Definition	Progressive TR	Asymptomatic severe TR	Symptomatic Severe TR
Valve Hemodynamics			
Color Doppler jet	Central jet <50% RA	Central jet ≥50% RA	
Doppler vena contracta width (cm)	<0.7cm	≥0.7cm	
Regurgitant volume (mL/beat)	<45mL	≥45mL	
ERO	<0.40cm^2	≥0.40cm^2	
		Dense continuous wave signal with triangular shape Hepatic vein systolic flow reversal	
Hemodynamic Consequences			
RV/RA dilation	None	Yes	
Elevated RA with "c-V" wave		Yes	
Clinical Symptoms and Presentation	None	Elevated venous pressure No symptoms	Elevated venous pressure Dyspnea on exertion, fatigue, ascites, edema

Management

Treatment of primary TR with medical management alone are poor. Management of secondary TR is of underlying pulmonary hypertension or myocardial disease. Surgery can be considered in a subset of patients with isolated primary or secondary TR (without pulmonary hypertension or dilated cardiomyopathy).

Treat heart failure, right or left-sided: diuretics, aldosterone antagonists.

Treat causes of pulmonary HTN (e.g. mitral stenosis or CTEPH).

TVR if: severe symptomatic primary TR OR asymptomatic w/ RV dilation/dysfunction
- For secondary severe TR, consider TVR if undergoing left-sided valve surgery OR if tricuspid annular dilation >4 cm and/or sx of right heart failure (Circ 2021;143:e)
- Isolated TV surgery a/w high mortality, although may be recommended for severe TR refractory to medical therapy
- Numerous transcatheter therapies are potential options but still lack long-term clinical outcome/performance data (JACC 2018;71:2935)

VASCULAR MEDICINE

Venous Thromboembolism
Deep Vein Thrombosis

A. Definition/ Classification

Clot formation within the deep venous system. Typically classified as:

- Proximal/ "above the knee" (external iliac, popliteal, femoral veins including superficial femoral)
- Distal/ "below the knee" (ant. tibial, post. tibial, peroneal, gastrocnemius and soleus vein)
- Upper extremity (includes the internal jugular vein)

B. Clinical Presentation

Patients may be asymptomatic or complain of unilateral leg pain, swelling, erythema, or warmth.

1. Always consider DVT in signs, symptoms and diagnosis of PE.

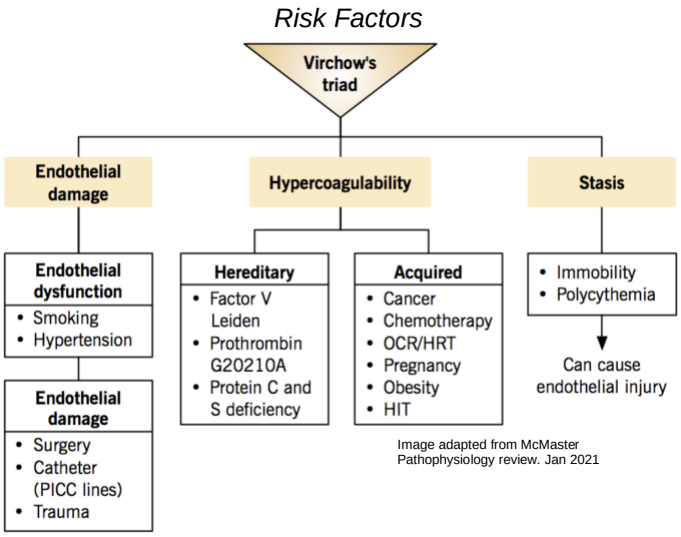


Image adapted from McMaster Pathophysiology review. Jan 2021

Anatomic risk factors

Iliac vein compression (aka "*May-Thurner syndrome"*): compression of the left iliac vein between the right iliac artery and lumbar spine within the deep pelvis. Compression on the right is also possible.

Effort induced thrombosis (aka "*Paget-Schroetter syndrome"*)*:* Upper extremity venous thrombosis usually due to underlying compressive anomaly at the thoracic outlet.

IVC abnormalities: Congenital venous malformations of the IVC that may lead to DVT. Primarily occurs in young patients

C. Diagnostics

- Diagnosis of an acute DVT in the lower extremity begins with an assessment of the pre-test probability for that patient and incorporates US and D-dimer based upon this pre-test probability assessment[1].
  - Consider Well's Criteria for DVT to risk stratify likelihood of DVT.
- Venous doppler US is the most practical test to make the diagnosis of DVT.

D. Management

- *Therapeutic anticoagulation is mainstay of treatment* in absence of contraindications (i.e. increased bleeding risk)
- **Always** indicated in patients with lower extremity proximal DVT, Upper extremity DVT, and in **some** cases of distal DVT
  - Proximal lower extremity DVTs are associated with a high risk of PE and mortality

1. **Medical therapy:**

- Direct oral anticoagulants (DOACs) (apixaban, rivaroxaban, edoxaban and dabigatran) are considered first-line agents for VTE in the majority of patients.
- Warfarin favored in patients with APLAS (TRAPS)[2].
- LMWH was considered the only preferred method of AC in active malignancy until recently where DOACs have shown to have similar safety and effectiveness in patients with active malignancy who do not have gastric cancer or gastroesophageal lesions (ASH 2021 Guideline)[3]

Agent	Mechanism	Indications	Dose
Unfractionated Heparin	Inactivates thrombin & factor Xa through AT-dependent mechanism	• Treatment of DVT/PE	**Treatment:** 80U/kg bolus + initiate gtt at 18U/kg/hr and titrate per protocol for goal PTT 70-100
Warfarin (Coumadin)	Vitamin K antagonist	• Treatment of DVT/PE	**Treatment**: Dose depends on INR measurements and varies for typical INR goal 2-3 *Requires bridging with parenteral agent if INR <2*
Apixaban (Eliquis)	Factor Xa inhibitor	• Treatment of DVT/PE • DVT prophylaxis after hip/knee replacement surgery • Reduction in risk of recurrent DVT/PE after 6 months of therapeutic anticoagulation	**Treatment**: 10 mg BID x 7 days, then 5 mg BID during the first 6 months, and 2.5 mg BID thereafter for most patients **Prophylaxis**: 2.5 mg BID
Rivaroxaban (Xarelto)	Factor Xa inhibitor		**Treatment**: 15 mg BID x 21 days, then 20 mg QD for the first 6 months, and 10 mg QD thereafter for most patients **Prophylaxis**: 10 mg QD *Should not be used in patients with CrCl <30 mL/min*
Edoxaban (Savaysa)	Factor Xa inhibitor	• Treatment of DVT/PE after 5-10 days of therapy with UFH/LMWH	**Treatment**: 60 mg QD (30 mg QD if CrCl 15-50 mL/min) **Prophylaxis**: Not approved
Dabigatran (Pradaxa)	Direct thrombin inhibitor	• Treatment of DVT/PE after 5-10 days of therapy with UFH/LMWH • DVT/PE prophylaxis after hip replacement surgery • Reduction in risk of recurrent DVT/PE following initial therapy	**Treatment**: 150 mg BID (CrCl >30 mL/min) **Prophylaxis**: 110 mg once, then 220 mg QD *Should not be used in patients with CrCl <30 mL/min*
Enoxaparin (Lovenox)	Activates ATIII to inactivate Xa > IIa	• Prophylaxis and treatment of DVT/PE	**Treatment:** 1 mg/kg BID or 1.5 mg/Kg QD **Prophylaxis**: 40 mg QD (30 mg BID if high-risk) *Should be used with caution in patients with reduced CrCl. Titration by anti-Xa may be useful*
Fondaparinux (Arixtra)	Activates ATIII to inactivate Xa only	• Prophylaxis and treatment of DVT/PE	**Treatment**: 5 mg QD (if <50 kg), 7.5 mg QD (if 50-100 kg), 10 mg QD (if >100 kg) **Prophylaxis**: 2.5 mg QD *Should not be used in patients with CrCl <30 mL/min*

Bivalirudin (Angiomax)	Direct Thrombin inhibitor	• Treatment of DVT/PE particularly in patients with HIT	**Treatment:** 0.15-0.2 mg/kg/hr (Dose reduction if CrCl<60 mL/min
Argatroban	Direct IIa inhibitor	• Treatment of DVT/PE particularly in patients with HIT	**Treatment**: 0.2-1 mcg/kg/min

- **Duration:**
  - First episode of provoked VTE: Minimum *of three months* of therapeutic anticoagulation[4].
  - If persistent risk factors (e.g. immobility, obesity, HRT) and low risk of bleeding: Minimum 6-12 months.
  - If unprovoked VTE, recurrent provoked VTE, active malignancy: Indefinite AC may be considered.
  - *Careful consideration of bleeding risk should always be considered when planning duration of therapy.*

2. **Catheter-directed thrombolysis (CDT):**

CDT is usually reserved for patients with phlegmasia cerulea dolens or highly symptomatic proximal clot (typically ilio-femoral).

- Suitable candidates should have fresh clot (<21 days old as organized clot is less likely to respond to lysis) and low bleeding risk.
- CDT may decrease post-thrombotic syndrome (PTS) incidence and severity, esp. w/acute ileo-femoral DVT. [5,6 7]

3. Inferior vena cava (IVC) filters:

IVC filters are not routinely inserted as a stand-alone or adjunctive therapy for patients with acute DVTs.

- IVC filters are considered in patients with acute DVTs and PE with **absolute** contraindications to AC (e.g., recent surgery, hemorrhagic stroke, active bleeding).
- IVC filters may be permanent or retrievable, although the latter have become increasingly popular due to the long-term complications associated with indwelling IVC filters (including filter migration, IVC wall penetration, and thrombosis).
- IVC filter retrieval should be considered once the contraindication to anticoagulation has resolved
- **In general, if an inpatient has IVC filter placed during admission, they should leave with an appointment scheduled for its removal.[8]**

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Pulmonary Embolism

A. Definitions

- **Acute:** acute obstruction within the pulmonary arteries by material (e.g. thrombus, tumor, air, fat) from elsewhere in the body
- **Chronic thromboembolic pulmonary hypertension (CTEPH):** symptomatic post-embolic pulmonary obstruction leading to pulmonary hypertension.

B. Clinical Presentation

- Presenting symptoms: dyspnea, tachypnea, chest pain, pleuritic pain, palpitations, pre-syncope, cough, hemoptysis, low grade fever, syncope, and cardiac arrest.
- Signs: tachycardia (sinus most common, also new RV strain patter, RAD), hypoxemia, hypotension; e/o LE DVT

Image from StatPearls Jan 2021

C. Diagnostics

- CT chest angiogram is the gold standard test to diagnose PE.
- V/Q scan is an alternative for those with contraindications.
- Consider Transthoracic echo (TTE) and lower extremity ultrasound (LENIs) for risk stratification.

Pre-test probability:

There are several externally validated scoring systems to assess for the pretest probability of pulmonary embolism.[9] They include the original Wells score, the Geneva score and the pulmonary embolism rule-out criteria (PERC) score[10].

1. Wells Criteria for PE [10,11,12] (100% Sn, 85% Sp) Highly sensitive when used to exclude the diagnosis of PE in patients with low clinical probability of PE (score ≤2). Critiques of the Wells score point to its subjective criteria that cannot otherwise be standardized across users.

2. Geneva score[10,13] Developed as an objective measurement of pre-test probability but has not been demonstrated to be superior to the Wells score.

3. PERC score[10,14] (97% SN, 22% Sp) To be used only in instances of low pre-test probability by either the Wells score or Geneva score.

Labs:
- *D-dimer* [15]: D-dimer has a high sensitivity (80%-100%) and low specificity (23%-63%). Obtain when the pre-test probability for PE is low (i.e., a rule **out test)**.
  - Can be elevated in many different diseases associated with fibrinolysis (cancer, inflammation/infection, DIC, arterial thrombus, aortic dissection, CHF, ESLD, and ESRD). Use Age-adjusted D-dimer[16] for patients >50 years of age (age x 10ng/mL = cut off value in ng/mL). Normal levels cut off to rule out PE is <500 ng/mL.

Imaging:
- **CTPE**[17] (98% sp, 86% sn) Most definitive diagnostic test. Contraindicated (relative) in pregnancy, renal insufficiency or contrast allergy.
- **V/Q scan**[17] (93% sp, 83% sn) Alternative image modality in those with contraindications to CTPE
- **LENI**[17] (86% sp, 44% sn): Obtained in conjunction with CTPE or V/Q scan or in some instances to aid in treatment decisions when chest imaging cannot be obtained promptly (e.g. pregnancy).
- **TTE**: Obtained with CTPE or V/Q scan. Utilized in risk stratification.

Risk Stratification
Risk stratification of PE depends on the presence or absence of **hemodynamic instability, increased respiratory effort** and **right heart strain**. Overall patient risk taken into context as well as alluded to in the PESI score
- RV strain can be assessed via multiple modalities
  - Cardiac biomarkers (NT-proBNP, hsTnT),
  - EKG (RBBB, R axis deviation, anterior T wave inversions, S1Q3T3),
  - CT-PE (RV/LV ratio >0.9), or
  - TTE (RV dilation, hypokinesis, or McConnell's sign [diffuse RV wall hypokinesis with apical sparing]).

Low Risk	Intermediate Risk Mortality risk (3-15%)	High Risk Mortality risk (>15%)
● No evidence of Right heart strain and no hemodynamic instability ● (Low risk PESI)	*Intermediate-low*: ● +biomarkers, RV dysfunction, **or** low PESI score (III-V) *Intermediate-high*: ● +Troponin **and** RV dysfunction on Echo or CT imaging	● Hemodynamic instability (SBP <90mmHg for >15mins) ● Cardiac arrest

- **NB**: the presence/ absence of hemodynamic instability does not always correlate with the anatomic location or the degree of clot burden.
- The Pulmonary Embolism Severity Index (PESI)[14] helps to risk stratify patients who can safely be treated outpatient once a diagnosis is made.

Management
Low risk: Initiate therapeutic oral AC provided there is no contraindications and risk of bleeding is low.
- If no other reason for hospitalization and adequate home support can discharge home, direct from ED

Intermediate risk: Initiate AC; monitor closely for clinical signs of deterioration. PERT c/s recommended.
- Generally recommended that most patients without hypotension are not treated with thrombolytic therapy.[4]
- Thrombolysis or catheter-based therapies can be considered weighing the risks and benefits of the procedure.
- If persistent dyspnea, consult PERT

High-risk:
*Consult PERT **ASAP***.
- Consider systemic thrombolysis decreased all-cause mortality but increased risk of major bleeding and intracranial hemorrhage[4]
- Catheter-directed thrombolysis

- For those with high bleeding risk, invasive stabilizing measures (e.g., ECMO) and surgical thrombectomy.

PERT: The Pulmonary Embolism Response Team (x47378) at MGH is a rapid response, multidisciplinary team that can be activated for prompt assessment and management of patients with intermediate to high-risk PEs.

Catheter-associated thrombosis

Clinical considerations

- Incidence as high as 14-18%.
- Duplex ultrasound is the diagnostic imaging modality of choice.
- Current guidelines recommended that systemic anticoagulation be administered for at least three months after the catheter has been removed.
- If central access is required, the CVC can remain in place as long as it is appropriately positioned and functioning correctly without evidence of infection.
- If the catheter remains for > 3 months on therapeutic AC, LMWH prophylaxis is recommended until the line is removed.[4]

Peripheral Artery Disease

A. Definition

Peripheral artery disease (PAD) is an atherosclerotic disease leading to peripheral artery stenosis or obstruction. PAD is prevalent worldwide and is estimated to affect 202 million people.[22]

- **Acute critical limb ischemia** is a sudden decrease in limb perfusion presenting within 2 weeks of an inciting event. Etiologies of arterial occlusion include thrombosis at site of atherosclerotic plaque in native artery (most common cause), thromboembolism, thrombosis of stent/graft, thrombosis of aneurysm, arterial dissection, and iatrogenic from arterial access sites.
- **Chronic limb ischemia** is ischemia of >2 weeks duration sufficient to threaten the limb. This typically corresponds to an arterial-brachial index (ABI) <0.4 usually due to multilevel > single vessel occlusions (i.e., aortoiliac and femoropopliteal vs isolated tibial vessel disease in diabetics)[23]

B. Risk Factors

Age ≥70 yo, Male, black, Smoking, DM, H/o Atherosclerosis, HTN, HLD, Elevated homocysteine

C. Clinical presentation

Classic claudication: exertional buttock, hip, thigh, calf, or foot pain that is relieved with rest.

Presentation	Percent of PAD pts ≥ 50 y.o.
Asymptomatic (screening)	20-50%
Atypical leg pain	40-50%
Classic claudication	10-35%
Threatened limb (ulceration, gangrene)	1-2%

- **Acute Critical Limb Ischemia**
  - 6 P's (**P**ain, **P**aresthesia, **P**aralysis, **P**oikilothermic (coolness), **P**allor, reduced **P**ulses
  - ABI <0.4 in conjunction with the above symptoms indicates severe ischemia

D. Diagnosis

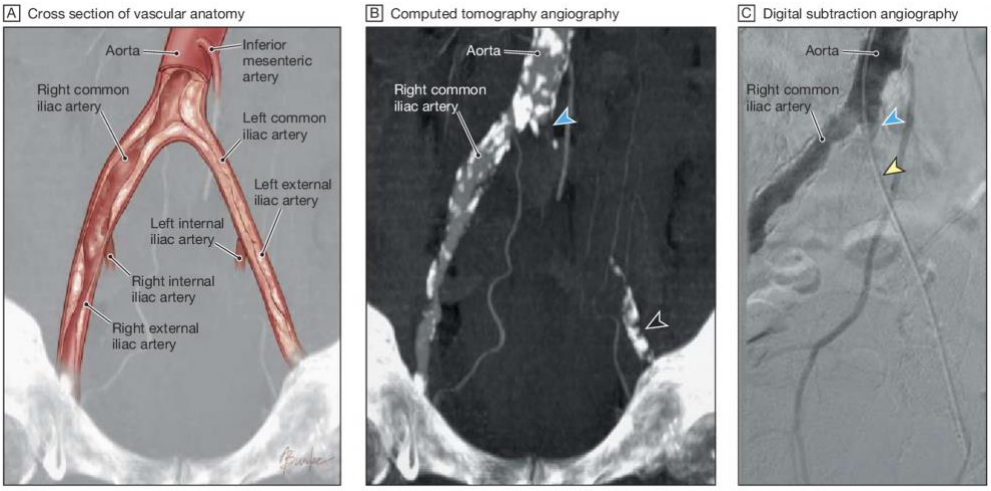
Screening

The USPSTF has stated there is insufficient evidence to recommend routine screening for PAD with an ABI.[24] However, the detection of PAD may identify patients at risk for atherosclerosis at other sites and can result in early interventions to lower overall CVD risk.

Diagnostics

The diagnosis of PAD can be suspected clinically based on history of symptoms, risk factors for PAD, and physical exam findings. Ankle-brachial index (ABI) should be used to confirm the diagnosis.

1. **ABI** (90% sn, 98% sp for detecting ≥ 50% stenosis.[24]
   a. < 1 indicates PAD. May be falsely elevated from calcifications and (e.g. in patients with DM)
2. **Segmental pressure and pulse volume recordings**
   a. Formal recordings using blood pressure cuffs and Doppler waveforms in the vascular lab
   b. Helpful for identifying site and severity of disease
3. **Exercise testing**
   a. Exercise adds sensitivity to inconclusive tests and should always be ordered as a component of ABI or segmental pressures (unless patients cannot negotiate the necessary walking component)
4. **Vascular imaging when anatomical information is required** (often before / after a procedure)



review and meta-analysis. Met et al JAMA 2009

a. Catheter-based arteriography - preferred imaging modality as it can be diagnostic and therapeutic.
   - CTA is highly specific/ sensitive. MRA accuracy is center dependent and may delay urgent intervention if concerned for critical ischemia.

b. Duplex US is a safe, cheap, alternative that is unfortunately under-utilized.

E. Management

Management of PAD: Management depends on presentation (asymptomatic, intermittent claudication or critical limb ischemia). Revascularization is an option for patients with significant or disabling symptoms unresponsive to other treatment options.

*Non-invasive therapy focused on **symptom relief***:

- Supervised Exercise Therapy: First-line treatment that improves walking time and distance. Supervised exercise is more effective and has a lower dropout rate.[25] It is comparable to stent revascularization in improving functional status and QOL and both better than medical therapy alone.[26]
- Cilostazol: Use for lifestyle-limiting claudication. Start 100 mg BID & titrate as tolerated. SE: HA, diarrhea, rhinitis. Contraindicated in the presence of systolic heart failure.

*Medical therapy focused on **lowering risk of PAD progression***:

- Risk factor modification: Aggressive DM & HTN management. Smoking cessation. Weight loss.
- Antiplatelet agents:
  - Aspirin 81 or clopidogrel 75 mg are first line agents. The benefits of these agents in PAD are unclear as recommendations for PAD have been extrapolated from studies in CVD.
  - DAPT is not recommended unless there is another indication due to increased bleeding risk without benefit.[27]
- Statin: Moderate and high-intensity statins provide reduction in cardiovascular events and may also improve symptoms.
- Rivaroxaban: The COMPASS trial showed that rivaroxaban (2.5mg BID) plus aspirin (100mg QD) led to lower risk of major adverse cardiovascular events but increased risk of major bleeding.[28] Rivaroxaban is typically offered to patients with evidence of atherosclerosis in multiple arterial beds.

Revascularization is recommended for patients with limb-threatening ischemia such as ischemic rest pain or ulceration and patients with significant or disabling symptoms unresponsive to above.[29] Options include percutaneous intervention or open surgical intervention depending on the location and extent of disease. Most patients are offered endovascular intervention.

Management of acute critical limb ischemia:

1. Immediate anticoagulation with heparin gtt
2. Place patient in “reverse Trendelenburg” if possible (to increase gravity dependent perfusion)
3. Revascularization
   a. *Factors that favor surgical revascularization*: immediately threatened limb, large proximal lesion, long segment lesion, diffuse multilevel disease
   b. *Factors that favor endovascular revascularization*: comorbidities that increase surgical risk, multi-level disease undergoing staged approach (endovascular-first), no suitable vessel for bypass graft
4. If irreversible ischemia (non-salvageable), amputation may be unavoidable

Clinical categories of acute critical limb ischemia[23]

Category	Clinical features	Doppler pulses	Management and Prognosis
Viable	No sensory loss or muscle weakness	Audible	No immediate threat of tissue loss Obtain vascular imaging
Marginally threatened	Minimal pain with no sensory loss and weakness	Arterial pulses inaudible Venous pulses audible	Need to be treated promptly, but salvageable Obtain vascular imaging
Immediately threatened	Sensory loss, rest pain, mild-to-moderate weakness	Arterial pulses inaudible Venous pulses audible	Need immediate revascularization (no time for imaging), but salvageable
Irreversibly ischemic	Tissue loss or nerve damage Profound sensory loss and weakness Paralysis or rigor possible	Inaudible	Require amputation, revascularization may allow for healing or lower amputation

Management of chronic limb ischemia:
A subset of patients can be treated with conservative management consisting of aggressive wound care, pain control, and medical management. However for most patients, intervention is recommended.

Options for revascularization include endovascular therapy or bypass surgery. There has been persistent, widespread clinical uncertainty about the best means by which to revascularize patients with chronic limb threatening ischemia. In modern practice most patients receive endovascular therapy first. The BEST-CLI trial is currently enrolling patients and is designed to compare best endovascular therapy with best open surgical treatment in patients eligible for both treatments.

Amputation may be considered in patients with sepsis, limb paralysis, uncorrectable flexion contracture, or significant necrosis of weight-bearing parts of the foot.

*Wound care consult and referral to wound clinic is **highly** recommended*

Renal Artery Stenosis

A. Definition: Renal artery stenosis (RAS) is characterized by narrowing of one or both renal arteries leading to impaired blood flow to the kidney resulting in a spectrum of clinical syndromes that range from asymptomatic obstruction (incidental RAS), renal vascular hypertension (RVH) and ischemic nephropathy.[30]

B. Risk Factors and Etiology: RAS likely accounts for 1-5% of patients with hypertension. Prevalence is higher in patients with acute, severe, or refractory HTN.[31] Risk factors include age, HLD, HTN, and elderly patients with comorbidities such as diabetes, PAD, or CAD.[32]
   1. Atherosclerotic RAS (ARAS) accounts for 90% of all RAS.[33] Patients with ARAS are likely to have atherosclerotic disease in other areas of the body including CAD and PAD.
   2. Fibromuscular Dysplasia (FMD) is a non-inflammatory, non-atherosclerotic vascular condition that commonly affects the renal arteries.[34] According to the FMD registry, the majority of patients affected with FMD are female (90%) and the mean age at diagnosis was 52 years.[35] In this registry FMD was identified in the renal artery in 66% of patients. Similar data exist in the international / European registry.
   3. Other non-atherosclerotic forms of RAS include aneurysms, congenital/ traumatic AV fistulas, vasculitis, neurofibromatosis, trauma, embolization, post-radiation therapy, dissection, and extrinsic compression of the renal arteries due to tumors.[36]

C. Clinical Presentation: Patients present with severe or resistant hypertension. Physical exam findings of include a unilateral systolic-diastolic abdominal/ flank bruit (Sn 40% Sp 99). Labs may show HypoK and metabolic acidosis. Suspect in non-obese patients <30 y.o. with no family history of HTN. RAS is associated with an unexplained rise in serum Cr > 50% within 1 week of ACE/ ARB initiation, however unilateral RAS is not a contraindication to these medications.

D. Diagnostics Testing for renovascular disease is indicated for patients who present with clinical findings consistent with secondary hypertension with moderate-high pre-test probability.

Study	Sens (%)	Spec (%)	Comments
Duplex Doppler US	84-98*	62-99*	Pros: No IV contrast; Inexpensive **For detecting stenosis >60%* Cons: Technically challenging and requires local expertise. Accessory renal arteries may be missed
CTA	86-93	90-100	Pros: Visualizes adjacent structures including accessory renal arteries; less time-consuming/operator-dependent Cons: Radiation; iodine contrast; difficult to eval severity in presence of significant calcification
MRA	94 vs 97 *(non vs gad-enhanced)*	85 vs 93 *(non vs gad-enhanced)*	Pros: A non-contrast MRA is an alternative to CTA in pts with renal insufficiency or allergy. Can assess renal perfusion using gad clearance Cons: $$$; quality is center-dependent, incompatible with some implanted medical devices; cannot evaluate in-stent restenosis, many patients cannot tolerate the small space in the machine
Arteriography			Pros: GOLD STANDARD if performed in conjunction with pressure measurements Cons: invasive, iodine contrast, risk of complications

Adapted from 2011 ACC/AHA Practice Guidelines for the Management of Patients with PA

E. Management

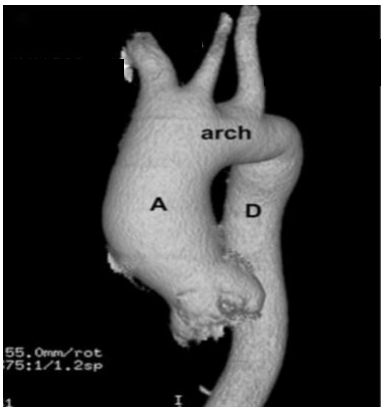
- Medical therapy remains the mainstay of treatment for RAS. Treatment focuses on lowering cardiovascular risk through smoking cessation, glucose control, cholesterol reduction, ASA, and blood pressure control. Choice of anti-HTN medication should follow published guidelines as if for non-RAS patients.
  - I*mportantly,* ACE and ARB are **not** contraindicated in RAS. ~50% of patients with RAS will usually have a mild increase in creatinine after the administration of an ACE/ARB. ACE/ARB may be of benefit given elevated RAAS activity in RAS.
- **Revascularization:** Options for revascularization include percutaneous angioplasty +/- stenting and surgical revascularization. Several RCT's, including, the CORAL trial demonstrated that renal artery stenting **plus** medical therapy did not confer a significant benefit with respect to the prevention of clinical events.[37] However, some patients do benefit from revascularization and it is recommended for those who have a high likelihood of benefit.[38] That includes patients with hemodynamically significant atherosclerotic RAS **AND** at least one of the following 1) recurrent "flash" decompensated HF; 2) refractory ACS; 3) typically new-onset resistant HTN; or 4) acutely progressive CKD stage IV. Revascularization strategy may vary depending on etiology of RAS (i.e., atherosclerotic RAS vs FMD).

Aortic Aneurysm

A. Definition

Thoracic Aortic Aneurysm (TAA): is a full-thickness dilation of a segment of the thoracic aorta that is at least 50% larger than the expected diameter of that segment. The normal aortic diameter varies according to age, sex, and body size. [39]

Abdominal Aortic Aneurysm (AAA): A full-thickness dilation of a segment of the abdominal aorta typically ≥3 cm. Classified by location (suprarenal, pararenal, or infrarenal) and morphology (fusiform vs saccular).[40,41]



CT image of ascending thoracic aortic aneurysm. *Adapted from JACC 2010;55:e27.*

B. Risk Factors

Thoracic Aortic Aneurysm (TAA):

Sporadic (Degenerative)	Genetically mediated
Hypertension (Most common. occurring in 60% of pts w/ TAA[2]) Male Age Smoking history Hypercholesterolemia Prior aortic dissection Aortitis (vasculitis/ infection)	Marfan syndrome Ehlers-Danlos syndrome Loeys-Dietz syndrome Turner syndrome Familial TAA & dissection Bicuspid aortic valve disease

Abdominal Aortic Aneurysm (AAA) [40]:

Risk Factors	Protective Factors
Older age Smoking history (>90% of pts with AAA[42]) First-degree relative with AAA History of other large vessel aneurysms Atherosclerosis Hypercholesterolemia Obesity Hypertension	African American heritage Asian heritage Hispanic ethnicity Diabetes Female sex

Risk of rupture:

TAA: The risk of rupture or dissection increases abruptly as thoracic aneurysms approach 6 cm because at this size, distensibility of the aorta rapidly falls. The annual risk of rupture is 2% for TAAs <5 cm and 7% for TAAs >6 cm.[43]

AAA: Risk of rupture increases with aneurysm size with <1% annual rupture risk for AAA <4 cm in diameter and >10% annual rupture risk for AAA >6 cm in diameter.[42] Rupture is often lethal with mortality cited as 85-90%[44]. Female sex appears to be an independent risk factor for rupture in AAA. Women make up ~20% of AAAs compared to men but constitute approximately ~30% of all AAA ruptures.[45]

C. Clinical Presentation

TAA and AAA are typically clinically silent, however, patients who are symptomatic can present with symptoms due to compression of surrounding structures.[46] Patients with

- Ascending aorta/aortic arch
  - Heart failure due to aortic regurgitation
  - Myocardial ischemia or infarction due to compression of a coronary artery
  - Dysphagia due to esophageal compression
  - Hoarseness due to left recurrent laryngeal nerve compression
  - Hemidiaphragmatic paralysis due to phrenic nerve compression
  - Wheezing, cough, dyspnea due to compression of the tracheobronchial tree
  - SVC syndrome
- Descending aorta: Back pain from erosion into the adjacent spine
- Abdominal: Pulsatile abdominal mass, Constant abdominal pain or back pain

D. Diagnosis

Typically, an incidental finding on imaging studies (e.g., CT, CXR, echo)

TAA:

1. CTA or MRA: Helpful in determining size and extent of the aneurysm. Patients with known connective tissue disease syndromes or first-degree relatives with TAA should undergo complete aortic imaging.[39]
2. TTE: Indicated when aortic root or ascending aortic aneurysm is present to evaluate for the presence of a bicuspid aortic valve and aortic regurgitation.

AAA:

1. Transabdominal US: Preferred for screening and surveillance of infra-renal AAA. Initial test if suspect AAA. High sensitivity at 98% and specificity of 99%[42].
2. CT imaging: Preferred for supra-renal AAA, stable symptomatic patients, preop planning and often post-op surveillance.

E. Management

TAA: The decision point for management rests on whether there is any indication for surgical repair. Repair options include open surgery or endovascular repair.

Indications for repair [47]	**Conservative Management** [46]
1. **Symptomatic TAA** 2. **Asymptomatic ascending TAA** with end-diastolic aortic diameter (EDAD) >5.5 cm **or** aortic size index ≥2.75 cm/m^2 3. **Asymptomatic ascending TAA** with (EDAD) >4.5 cm *if undergoing aortic valve surgery* 4. **Asymptomatic descending TAA** if Aortic diameter >5.5 cm 5. **Asymptomatic TAA** with growth rate >0.5 cm/year 6. **Asymptomatic TAA** in hereditary conditions	*Risk factor modification* 1. Smoking cessation 2. Statin therapy for HLD 3. Aggressive blood pressure control ● Goal SBP 105-120 mm Hg ● Beta blockers are preferred give decreases decreasing aortic shear stress. *Avoid fluoroquinolones as they have been linked to an increased risk of aortic aneurysm or dissection.[48]

AAA: Options for repair include open surgical repair or endovascular repair (EVAR) if indicated. EVAR 1, DREAM, OVER all show initial survival benefit with EVAR but similar long-term mortality at 8-10 years. Patients who undergo EVAR require long-term surveillance with CT for development of endoleaks[49,50].

Indications for Repair [42]	**Conservative Management** [49,50]
1. Symptomatic AAA **2. Asymptomatic AAA** if - Diameter ≥5.5 cm - Saccular abdominal aneurysms may be repaired at smaller diameters. - Rapid growth rate - Distal embolization of aneurysm material (mural thrombus)	Medical management is focused on preventing further enlargement. ● Smoking cessation (only intervention proven to reduce rate of AAA growth ● Aggressive HTN and HLD treatment ● No clear evidence that pharmacotherapy reduce AAA growth (statins, beta blockers, ACE inhibitors)

F. Surveillance

***TAA*:** Asymptomatic patients with thoracic aortic aneurysm who do not meet indications for repair should undergo long-term monitoring. Imaging modalities used for surveillance include TTE, CTA, or MRA.

Surveillance Recommendations for TAA[47]

Type of Aneurysm	Size	Surveillance timing
Aortic root or ascending aorta		
Sporadic	3.5-4.4 cm 4.5-5.4 cm	Annual Every 6 months
Genetically mediated	3.5-4.4 cm 4.5-5.0 cm	Annual Every 6 months
Descending aorta	4.0-5.0 cm 5.0-6.0 cm	Annual Every 6 months

AAA: **The U.S. Preventive Services Task Force (USPSTF) recommends a one-time screening by abdominal ultrasound for men aged 65 to 75 years who have ever smoked** Society guidelines also recommend ultrasound screening for AAA in first-degree relatives of patients with AAA who are >65 years of age.[43,51] Once detected, it is recommended that monitoring continue until aneurysm diameter exceeds 5.5 cm.

Surveillance Recommendations for AAA[43]

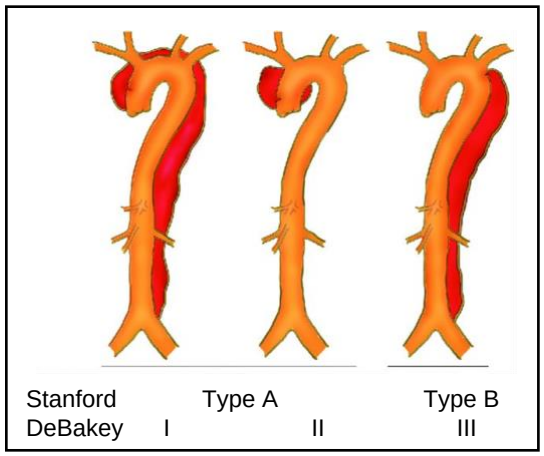
Aneurysm size	Surveillance timing
3.0-3.9 cm	Every 2-3 years
4.0-4.9 cm	Every 12 months
5.0-5.4 cm	Every 6 months

Aortic Dissection

A. Definition

Tearing of the aortic intima resulting in separation of the arterial wall into two layers forming a false lumen that can propagate both distally and less commonly in a retrograde fashion. The Stanford system is the most widely used classification system that guide management decisions.

Type A: Dissection involves the ascending +/- descending aorta.
Type B: Dissection involves only the descending aorta.
Duration: acute (<2 weeks) vs chronic (>2 weeks)



Aortic dissection classifications. *Adapted from Ital J Vasc End Surg 2015;22:141.*

B. Risk Factors

Hypertension, collagen disorders (Marfan Syndrome, Ehlers-Danlos Syndrome type IV, Loeys-Dietz Syndrome, aortic surgery/ instrumentation (CABG, coronary cath, TAVR), preexisting aortic aneurysm, congenital heart defects (bicuspid aortic valve, aortic coarctation), and pregnancy.

C. Clinical Presentation

- ***Symptoms:*** Ripping/ tearing chest pain, inter-scapular back pain, abdominal or per umbilical pain (may be migratory as dissection propagates caudally), hypertension, hypotension, syncope, AMS.
- ***Physical exam****:* Asymmetric BP (SBP variation >20 mm Hg between arms) or pulse deficit
- ***Image findings*****:** CXR with mediastinal widening on CXR (60-90% of cases). EKG findings are 31% normal, 42% nonspecific ST-T changes, 15% ischemia, and 5% acute MI

Complications of aortic dissection are mainly from propagation and include aortic valve regurgitation, cardiac tamponade, obstruction of coronary artery ostia, coronary artery dissection, and end-organ failure due to abdominal aortic branch vessel obstruction.

End organ complications	Presentation
Acute MI (RCA most common[53])	Chest pain; ST-T changes, + trop
Acute stroke	Focal neurologic deficits, headache
Spinal cord ischemia	Acute paraplegia
Mesenteric ischemia	Abdominal pain, bloody diarrhea,
Limb ischemia	6 P's (pallor, paresthesia, pain etc.)

D. Diagnostics

Imaging remains the mainstay of diagnosis. Diagnostic tools have been developed to better predict likelihood of aortic dissection given variable nature of presentation.

D-dimer: Recent studies have demonstrated that a D-dimer <500ng/mL can effectively identify patients who **do not** have acute aortic dissection. (97% sn, 56% sp, 96% NPV).[54]

Imaging: CTA most common initial test. If the patient is hemodynamically unstable, TEE. (98% sn & 63-96% sp).

Study	Sens (%)	Spec (%)	Comment
CXR	68-90	n/a	Mediastinal widening (64%), displaced intimal calcification (9%), pleural effusion (16%), abnl aortic contour (76%), normal (12%)
TTE	30-80	83-96	Pros: Useful for complications: AI, tamponade, LV, valves Cons: Only proximal aorta is visualized
Chest CTA*	97-100	83-100	Pros: Available, fast and holistic evaluation of chest Cons: IV contrast, cannot evaluate coronaries or aortic valve reliably, site of tear often not defined
MRA	98-100	87-100	Pros: Test of choice for following chronic dissection Cons: Long image acquisition time

TEE	97-100	98-100	If high pretest probability and chest CTA contraindicated. Evaluate LV, AV, prox coronaries, and pericardial effusion

*Consider ordering CTA chest with neck, abdomen, pelvis w/ leg run offs
**Surveillance imaging should be obtained at 3, 6, 12 months and annually thereafter.

E. Management

Acute management consists of the following:

- **Access:** A-line in arm with highest pressure. Frequent BP checks of both sides; CVC; intubate
  - Rule out tamponade / CHF, then volume resus take emergently to the OR.
- **Goal HR <60**: IV BB (e.g., labetalol, esmolol). Reduce HR **before** blood pressure to prevent reflex tachycardia/ inotropy and minimize shear stress. CCB may be used as an alternative
  - Caveat: reducing HR in the setting of acute *severe* AI will increase the diastole/systole ratio, may precipitate cardiogenic shock.
- **Goal SBP 100-120 mmHg**: If SBP remains elevated **after appropriate HR control,** antihypertensive drip should be started (nitroprusside or nicardipine)
  - Avoid use of hydralazine - can increase hydraulic shear
- **Urgent surgical consultation should be considered for all patients**
  - Type A Dissection: **Stat page CT surgery.** Typically treated surgically with sternotomy, aortic root replacement with graft +/- valve repair/replacement since they are at high risk for complications.
    - If untreated, mortality is 1-2%/hour for the 48hrs in acute proximal dissections.
    - Surgery: mortality is 10-20%; medical therapy only: mortality is >50%.[55]
  - Type B Dissection: usually treated medically. Surgical interventions are reserved for patients who develop complications related to the dissection.

Agents used in the acute management of aortic dissection

Agent	Initial Dose	Comment
Labetalol	20-80 mg IV bolus 0.5-2 mg/min gtt	Can be used as a single agent Preferred PO agent
Propranolol	1-10 mg IV load 3 mg/h gtt	May be a more potent beta-blocker than esmolol
Esmolol	250-500 mcg/kg IV 25-200 mcg/kg/min gtt	Preferable in acute setting due to short half-life Better tolerated in pts with asthma or CHF
Diltiazem	20 mg bolus 5-15 mg/h gtt	Useful when BB contraindicated Avoid if reduced LVEF (can precipitate shock)
Nitroprusside	0.25-0.5 mcg/kg/min gtt	Use after BB to prevent reflex tachycardia minimize shear stress
Nicardipine	2.5-15 mg/hr gtt	

References

1. Wells, P. S., Anderson, D. R., Bormanis, J et al. (1997). Value of assessment of pretest probability of deep-vein thrombosis in clinical management. *The Lancet*, *350*(9094), 1795–1798. https://doi.org/10.1016/s0140-6736(97)08140-3
2. Pengo V, Denas G, Zoppellaro G, et al. Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome. *Blood*. 2018;132(13):1365-1371. doi:10.1182/blood-2018-04-848333
3. Lyman, GH, Carrier M, AY C, et al. American Society of Hematology 2021 guideline for management of venous thromboembolism: Prevention and treatment in patients with cancer. Blood Adv. 2021;5(4):927-974. (2021). *Blood advances,* 5(7), 1953-1953.
   Doi:10.1182/blood advances.2021004734
4. Kearon, C., Akl, E. A., Ornelas, J., et al. (2016). Antithrombotic Therapy for VTE Disease. *Chest*, *149*(2), 315–352. https://doi.org/10.1016/j.chest.2015.11.026
5. Enden, T., Haig, Y., Kløw, N.-E., et al. (2012). Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. *The Lancet*, *379*(9810), 31–38. https://doi.org/10.1016/s0140-6736(11)61753-4
6. Vedantham, S., Goldhaber, S. Z., Julian, et al. (2017). Pharmacomechanical Catheter-Directed Thrombolysis for Deep-Vein Thrombosis. *New England Journal of Medicine*, *377*(23), 2240–2252. https://doi.org/10.1056/nejmoa1615066
7. Comerota, A. J., Kearon, C., Gu, et al. (2019). Endovascular Thrombus Removal for Acute Iliofemoral Deep Vein Thrombosis. *Circulation*, *139*(9), 1162–1173. https://doi.org/10.1161/CIRCULATIONAHA.118.037425
8. Holly, B. P., Funaki, B., & Lessne, M. L. (2018). Inferior Vena Cava Filters. *Clinics in Chest Medicine*, *39*(3), 645–650. https://doi.org/10.1016/j.ccm.2018.04.015
9. Squizzato, A., Donadini, M. P., Galli, L., et al. (2012). Prognostic clinical prediction rules to identify a low-risk pulmonary embolism: a systematic review and meta-analysis. *Journal of Thrombosis and Haemostasis*, *10*(7), 1276–1290. https://doi.org/10.1111/j.1538-7836.2012.04739.x
10. Kline, J. A., Courtney, D. M., Kabrhel, et al. (2008). Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. *Journal of Thrombosis and Haemostasis*, *6*(5), 772–780. https://doi.org/10.1111/j.1538-7836.2008.02944.x
11. Anderson, D., Rodger, M., Ginsberg, et al. (2000). Derivation of a Simple Clinical Model to Categorize Patients Probability of Pulmonary Embolism: Increasing the Models Utility with the SimpliRED D-dimer. *Thrombosis and Haemostasis*, *83*(03), 416–420. https://doi.org/10.1055/s-0037-1613830
12. Khetpal, R., & Shibli, M. H. (2010). Predictability of Wells Score for the Diagnosis of Acute Pulmonary Embolism. *Chest*, *138*(4), 938A. https://doi.org/10.1378/chest.10949
13. Le Gal, G., Righini, M., Roy, P.-M., et al. (2006). Prediction of Pulmonary Embolism in the Emergency Department: The Revised Geneva Score. *Annals of Internal Medicine*, *144*(3), 165. https://doi.org/10.7326/0003-4819-144-3-200602070-00004
14. Aujesky, D., Obrosky, D. S., Stone, R. A., et al. (2005). Derivation and Validation of a Prognostic Model for Pulmonary Embolism. *American Journal of Respiratory and Critical Care Medicine*, *172*(8), 1041–1046. https://doi.org/10.1164/rccm.200506-862oc
15. Crawford F, Andras A, Welch K, et al. D-dimer test for excluding the diagnosis of pulmonary embolism. Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD010864. DOI: 10.1002/14651858.CD010864.pub2. Accessed 10 February 2021
16. Schouten Henrike J, Geersing G J, Koek H L et al. Diagnostic accuracy of conventional or age adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis *BMJ* 2013; 346 :f2492
17. Moore, A. J. E., Wachsmann, J., et al. (2018). Imaging of acute pulmonary embolism: an update. *Cardiovascular Diagnosis and Therapy*, *8*(3), 225–243. https://doi.org/10.21037/cdt.2017.12.01
18. Chatterjee, S., Chakraborty, A., Weinberg, I., et al. (2014). Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage. *JAMA*, *311*(23), 2414. https://doi.org/10.1001/jama.2014.5990
19. Wells PS, Hirsh J, Anderson DR, et al. Accuracy of clinical assessment of deep-vein thrombosis. Lancet. 1995 May 27;345(8961):1326-30. doi: 10.1016/s0140-6736(95)92535-x. Erratum in: Lancet 1995 Aug 19;346(8973):516. PMID: 7752753.
20. Haller, E. P., Nestler, D. M., Campbell, et al. (2014). Point-of-Care Ultrasound Findings of Acute Pulmonary Embolism: McConnell Sign in Emergency Medicine. *The Journal of Emergency Medicine*, *47*(1), e19–e21. https://doi.org/10.1016/j.jemermed.2014.01.032
21. Mismetti, P., Laporte, S., Pellerin, et al. (2015). Effect of a Retrievable Inferior Vena Cava Filter Plus Anticoagulation vs Anticoagulation Alone on Risk of Recurrent Pulmonary Embolism. *JAMA*, *313*(16), 1627. https://doi.org/10.1001/jama.2015.3780
22. Fowkes FG et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet. 2013;382(9901):1329-40.

23. Hirsh AT et al. ACC/AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic). Circulation. 2006;113(11):e463-654.
24. USPTF. Screening for Peripheral Artery Disease and Cardiovascular Disease Risk Assessment With the Ankle-Brachial Index: US Preventive Services Task Force Recommendation Statement. JAMA. 2016;320(2):177-183
25. Vemulapalli S et al. Supervised vs unsupervised exercise for intermittent claudication: A systematic review and meta-analysis. Am Heart J. 2015;169(6):924-937.
26. Murphy TP et al. Supervised Exercise, Stent Revascularization, or Medical Therapy for Claudication Due to Aortoiliac Peripheral Artery Disease: A Randomized Clinical Trial. J Am Coll Cardiol. 2015;65(10):999-1009
27. Bhatt DL et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med. 2006;354(16):1706-17
28. Eikelboom JW et al. Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease. N Engl J Med. 2017;377(14):1319-1330
29. Norgren L et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg. 2017;S5067
30. Tafur-Soto JD et al. Renal artery stenosis. Cardiology Clinics 2015;33(1):59-73.
31. Gupta R et al. Renal artery stenosis: new findings from the CORAL trial. Curr Cardiol Repo. 2017;19:75.
32. Hansen KJ et al. Prevalence of renovascular disease in the elderly: a population-based study. J Vasc Surg. 2002;36(3):443–451.
33. Safian RD et al. Renal-artery stenosis. N Engl J Med. 2001;344(6):431–442.
34. Olin JW et al. Fibromuscular dysplasia: State of the science and critical unanswered questions: A scientific statement from the American Heart Association. Circulation 2014;129:1048-78.
35. Olin JW et al. The United States registry for fibromuscular dysplasia: Results in the first 447 patients. Circulation 2012;125(25):3182-90.
36. Garovic VD et al. Renovascular hypertension: Balancing the controversies in diagnosis and treatment. Cleveland Clinic J of Med. 2005;72(12): 1135–1146.
37. Cooper CJ et al. Stenting and medical therapy for atherosclerotic renal artery stenosis. NEJM 2014;370:13-22.
38. Prince M et al. When and how should we revascularize patients with atherosclerotic renal artery stenosis? JACC Cardiovasc Interv 2019;12(6):505-17.
39. Elefteriades JA et al. Thoracic aortic aneurysm: Clinically pertinent controversies and uncertainties. JACC 2010; 55:841-57.
40. Kent, KC, et al. Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. J Vasc Surg. 2010; 52:539-48.
41. Lederle, FA et al. Prevalence and associations of abdominal aortic aneurysm detected through screening. Aneurysm detection and management (ADAM) veterans' affairs cooperative study group. Ann Intern Med.1997;126:441-9.
42. Chaikof EL, et al. The society for vascular surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. J Vasc Surg. 2018; 67:2-77.
43. Davies RR, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg 2002; 73:17-28.
44. Coady MA, et al. Familial patterns of thoracic aortic aneurysms. Arch Surg 1999; 134:361-7.
45. Vouyouka AG et al. Arterial vascular disease in women. J Vasc Surg. 2007; 46:1295-1302.
46. Isselbacher EM. Thoracic and abdominal aortic aneurysms. Circulation 2005; 111:816-28.
47. Hiratzka LF et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. JACC 2010; 55:e27-129.
48. Pasternak B et al. Fluoroquinolone use and risk of aortic aneurysm and dissection: nationwide cohort study. BMJ 2018; 360:k6
49. The United Kingdom EVAR trial investigators. Endovascular versus open repair of abdominal aortic aneurysm. NEJM. 2010; 362:1863-71.
50. The UK small aneurysm trial participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. Lancet. 1998; 352:1649-55.
51. Norman PE, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. BMJ. 2004; 329:1259-64.
52. Bickerstaff LK, et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982;92:1103-8.
53. Lentini et al. Aortic dissection with concomitant acute myocardial infarction: From diagnosis to management. J Emerg Trauma Shock. 2011; 4:273-8
54. Shimony A, Filion KB, Mottillo S, Dourian T, Eisenberg MJ. Meta-analysis of usefulness of d-dimer to diagnose acute aortic dissection. Am J Cardiol. 2011 Apr 15;107(8):1227-34. doi: 10.1016/j.amjcard.2010.12.027. Epub 2011 Feb 4. PMID: 21296332.
55. Nienaber et al. Aortic dissection: new frontiers in diagnosis and management. Circ. 2003; 108: 628–635
56. Nazerian P, Mueller C, Soeiro AM, Leidel BA, Salvadeo SAT, Giachino F, Vanni S, Grimm K, Oliveira MT Jr, Pivetta E, Lupia E, Grifoni S, Morello F; ADvISED Investigators. Diagnostic Accuracy of the Aortic Dissection Detection Risk Score Plus D-Dimer for Acute Aortic Syndromes: The ADvISED Prospective Multicenter Study.

Circulation. 2018 Jan 16;137(3):250-258. doi: 10.1161/CIRCULATIONAHA.117.029457. Epub 2017 Oct 13. PMID: 29030346

57. Cigarroa et al. Diagnostic imaging in the evaluation of suspected aortic dissection. Old standards and new directions. NEJM 1993; 328: 35–43

Quick Reference Guide: Vascular Medicine

Deep Vein Thrombosis (DVT)

- Therapeutic anticoagulation is indicated in all patients with proximal lower-extremity DVT (arising in the popliteal, femoral, or iliac veins) and in some cases of distal DVT, in the absence of contraindications
- Therapeutic AC should also be considered in cases of upper extremity DVT. Most of these cases are secondary to indwelling catheters
- DOACs are considered first-line agents for VTE in the majority of patients
    - Warfarin is favored in patients with APLAS
    - DOACs and Lovenox preferred in malignancy
    - When possible, prefer LMWH over UFH
- *Regarding duration of therapy:*
    - Most patients with a first episode of provoked VTE should receive at least **3 months** of therapeutic AC
    - Patients with low risk of bleeding and persistent risk factors (e.g., immobility or hormone replacement therapy) should be treated with an extended course (i.e., 6-12 months)
    - Long-term AC should be considered in select populations (Patients with unprovoked DVT/PE, Recurrent provoked DVT/PE, or Active malignancy)
- The only widely accepted indication for catheter-directed thrombolysis (CDT) for lower extremity DVT is proximal (typically ilio-femoral) clot leading to compromised lower extremity perfusion and risk of limb ischemia (i.e., phlegmasia cerulea dolens)
- IVC filters are indicated for patients with DVT who have an absolute contraindication to AC in order to decrease risk of PE.

Pulmonary Embolism (PE)

- Risk stratification of PE depends on the presence or absence of hemodynamic instability and right heart strain
    - RV strain can be assessed via multiple modalities including cardiac biomarkers (NT-proBNP, hsTnT), EKG (RBBB, anterior T wave inversions, S1Q3T3), CT-PE (RV/LV ratio >0.9), or TTE (RV dilation, hypokinesis, or McConnell's sign, in which there is diffuse RV wall hypokinesis with apical sparing)
- Based on the above, PE is generally classified as low-risk, intermediate-risk (e.g., submassive), and high-risk (e.g., massive)
- The MGH Pulmonary Embolism Response Team **(PERT, x47378)** is a multidisciplinary team that can be activated for prompt assessment and management of PE
    - Consult PERT in all cases of massive and select cases of submassive PE
- Intermediate-risk or submassive PE is characterized by right heart strain without hemodynamic instability. Prompt initiation of AC and ongoing monitoring is imperative.
- High-risk or massive PE is characterized by the presence of hemodynamic instability and carries significant risk of mortality. **CONSULT PERT** for consideration of tPA, thrombectomy, catheter directed thrombolysis, surgical embolectomy and ECMO
    - Administration of systemic thrombolytics (alteplase [t-PA] and Tenecteplase) is associated with decreased all-cause mortality

Peripheral Artery Disease

- The diagnosis of PAD can be suspected clinically based on history of symptoms, risk factors for PAD, and physical exam findings
- Diagnosis should be confirmed with ankle-brachial index (ABI)
    - ABI < 1 indicates PAD,
- Stable PAD is generally managed with exercise and risk-factor modification
- ASA 81 or clopidogrel 75 mg daily are often used as first-line agents in PAD
- Statins provide a reduction in systemic and limb arterial events and may also improve symptoms
- Medications such as cilostazol are used for lifestyle-limiting claudication
- Revascularization is an option for patients with significant or disabling symptoms unresponsive to other treatment options

Acute Critical Limb Ischemia

- This is defined as a sudden decrease in limb perfusion presenting within 2 weeks of an inciting event. Etiologies of arterial occlusion include thrombosis at site of atherosclerotic plaque in native artery (most common cause), thromboembolism, thrombosis of stent/graft, thrombosis of aneurysm, arterial dissection, and iatrogenic from arterial access sites
- Management involves immediate anticoagulation with a heparin gtt and revascularization (either endovascular or surgical)
- If irreversible ischemia (non-salvageable), amputation is recommended

Chronic Critical Limb Ischemia

- Clinically presents as rest pain and / or non-healing wound and / or gangrene
- Typically corresponds to ABI <0.4 and is defined as ischemia of >2 weeks duration sufficient to threaten the limb
- Most patients will require revascularization with either endovascular therapy (percutaneous transluminal angioplasty) or bypass surgery
- Adjunctive measures include aggressive wound care, pain control, and medical management
- Amputation may be indicated in patients with sepsis, uncontrolled pain or as a result of a multidisciplinary decision for patients who are otherwise debilitated.

Renal Artery Stenosis

- Renal artery stenosis (RAS) is characterized by narrowing of one or both renal arteries and accounts for an important cause of secondary HTN.)
- Atherosclerotic RAS (ARAS) accounts for 90% of all RAS
- Fibromuscular Dysplasia (FMD), a non-inflammatory, non-atherosclerotic vascular disease, commonly affects the renal arteries (66% of patients)
- Testing for RAS should only be pursued in patients thought to have a high likelihood of benefitting from revascularization
- Diagnostic/imaging modalities include: US, CTA, MRA, and arteriography
- Medical therapy and risk modification remains the mainstay of treatment for RAS
    - Choice of anti-HTN medication should follow published guidelines as if for non-RAS patients. Importantly, ACE and ARB are not contraindicated
- Options for revascularization include percutaneous angioplasty +/- stenting and surgical revascularization.

Thoracic Aortic Aneurysm

- Aneurysms are classified by their location (ascending aorta, aortic arch, descending thoracic aorta) and morphology (fusiform vs saccular)
- The majority of TAAs are sporadic (degenerative) and are associated with risk factors for atherosclerosis
- The natural history of TAA is characterized by slow expansion with progressive increase in risk of dissection as the aortic size increases
    - The risk of rupture or dissection increases abruptly as thoracic aneurysms approach 6 cm
    - The annual risk of rupture is 2% for TAAs <5 cm and 7% for TAAs >6 cm
- TAA is typically incidental diagnosed on imaging (CXR or TTE)
    - Further evaluation using CTA/ MRA is recommended to determine the size and extent of the aneurysm
    - When aortic root or ascending aortic aneurysm is present, TTE should be performed to evaluate for the presence of a bicuspid aortic valve
- Indications for repair include:
    - Symptomatic ascending and descending TAA (MI, CHF, back pain, paresthesia)
    - Asymptomatic ascending TAA
        - End-diastolic aortic diameter >5.5 cm or aortic size index ≥2.75 cm/m^2
        - End-diastolic aortic diameter >4.5 cm if undergoing aortic valve surgery
    - Asymptomatic descending TAA
        - Aortic diameter >5.5 cm or Aortic diameter ≥6 cm if high surgical risk
    - Asymptomatic TAA with growth rate >0.5 cm/year
    - Asymptomatic TAA associated with genetically mediated conditions
- Repair options include open surgery or endovascular repair
- For asymptomatic patients without an indication for repair, conservative management and surveillance is recommended to prevent rupture or dissection.
    - Risk factor modification (smoking cessation, statin therapy)
    - Blood pressure control with goal SBP 105-120 mm Hg
    - Surveillance (Frequency depends on etiology, location, size, and growth rate)

Abdominal Aortic Aneurysm

- The natural history is marked by progressive dilation over time
    - Risk of rupture increases with aneurysm size with <1% annual rupture risk for AAA <4 cm in diameter and >10% annual rupture risk for AAA >6 cm in diameter
    - Rupture is often lethal with mortality cited as high as 85-90%
- AAA are often detected incidentally on imaging studies performed for an alternative indication or through screening initiatives

    - The *USPSTF **recommends** one-time screening by abdominal ultrasound for men aged 65 to 75 years who have ever smoked (i.e., 100 or more lifetime cigarettes)*
- Patients with AAA are often asymptomatic but may present with a sensation of pulsation near the umbilicus, constant abdominal or back pain.
    - The classic triad of ruptured AAA (severe acute pain, pulsatile abdominal mass, and hypotension) is present in only 50% of cases
- In stable patients with a high suspicion for ruptured AAA, CT aortography is the initial test of choice
- In patients who presents with *abdominal or back pain and some suspicion for AAA*, abdominal ultrasound is the initial test of choice
- Indications for repair include:
    - Symptomatic AAA regardless of diameter
    - Asymptomatic AAA if Diameter ≥5.5 cm, Saccular abdominal aneurysms, Rapid growth rate
- Repair options include open surgical repair or endovascular repair (EVAR)
- Medical management is focused on risk modification
    - There is no clear evidence that pharmacotherapy (statins, beta blockers, ACE inhibitors) reduce AAA growth
- Surveillance imaging should be performed using transabdominal ultrasound

Aortic Dissection

- Aortic dissection occurs when a tear in the aortic intima exposes the medial layer to the systemic pressure of intraluminal blood
    - Type A dissections involve the ascending +/- descending aorta. Type B dissections involve only the descending aorta
- Risk factors for aortic dissection include HTN (most common), cocaine, heavy lifting, pregnancy, collagen disorders (Marfans/ Ehlers Danlos type IV), and prior aorta surgery/ minimally invasive intervention.
- Most patients with aortic dissection present with abrupt-onset severe, sharp chest pain that can radiate to the back
    - Exam findings include a pulse deficit, SBP variation >20 mm Hg between arms, and findings associated with complications/distal propagation
    - Complications include: Acute AI, tamponade, and end-organ ischemia secondary to branch-vessel involvement
- CTA is the most commonly performed imaging modality available
    - If hemodynamically unstable, TEE is the preferred diagnostic test given its high sensitivity and specificity
    - The addition of a negative D-dimer <500ng/mL can help to effectively rule-out dissection in addition to low ADD-RS score (<1)
- Type A dissections require emergent surgical evaluation for consideration of sternotomy and aortic root replacement with graft +/- valve repair/replacement. *PAGE CT SURGERY*
- In contrast, Type B dissections are typically managed medically with surgical intervention reserved for patients who develop critical complications
    - Use IV beta blockers **first** to aggressively reduce HR to goal <60 (reduces reflex tachycardia and decreases shear stress)
    - Once HR goal achieved, use vasodilators (nitroprusside, nicardipine) to reduce SBP (goal SBP 100-120 mm Hg)
- Longer-term management of Type B dissection involves ongoing therapy with anti-hypertensives (goal BP <120/80) to reduce incidence of late complications
    - Beta blockers or nondihydropyridine CCB and ACE are preferred over hydralazine

Congenital Heart Disease

Anatomic and Physiologic Classification System

The 2018 ACC/AHA Adult Congenital Heart Disease (ACHD) guidelines presented a new classification system (1). The ACHD anatomic and physiological (ACHD AP) classification system uses both anatomic complexity and physiologic/functional status.

- Anatomic classification:
  - Class I (simple)
  - Class II (moderate complexity)
  - Class III (great complexity)
- Physiological classification:
  - stages A-D (similar to the NYHA heart failure classification system)
  - considers patient's functional status and presence of valve disease, pulmonary hypertension, arrhythmias, aortic dilatation, end-organ function, or cyanosis.

Class I: Simple

Native disease
- Isolated small ASD
- Isolated small VSD
- Mild isolated pulmonic stenosis

Repaired conditions
- Previously ligated or occluded ductus arteriosus
- Repaired secundum ASD or sinus venosus defect without significant residual shunt or chamber enlargement
- Repaired VSD without significant residual shunt or chamber enlargement

Class II: Moderate Complexity

Repaired or unrepaired conditions
- Aorto-left ventricular fistula
- Anomalous pulmonary venous connection, partial or total
- Anomalous coronary artery arising from the pulmonary artery
- Anomalous aortic origin of a coronary artery from the opposite sinus
- AVSD (partial or complete, including primum ASD)
- Congenital aortic valve disease
- Congenital mitral valve disease
- Coarctation of the aorta
- Ebstein anomaly (disease spectrum includes mild, moderate, and severe variations)
- Infundibular right ventricular outflow obstruction
- Ostium primum ASD
- Moderate and large unrepaired secundum ASD
- Moderate and large persistently patent ductus arteriosus
- Pulmonary valve regurgitation (moderate or greater)
- Pulmonary valve stenosis (moderate or greater)
- Peripheral pulmonary stenosis
- Sinus of Valsalva fistula/aneurysm
- Sinus venosus defect
- Subvalvar aortic stenosis (excluding HCM; HCM not addressed in these guidelines)
- Supravalvar aortic stenosis
- Straddling atrioventricular valve
- Repaired tetralogy of Fallot
- VSD with associated abnormality and/or moderate or greater shunt

Class III: Great Complexity

- Cyanotic congenital heart defect (unrepaired or palliated, all forms)
- Double-outlet ventricle
- Fontan procedure
- Interrupted aortic arch
- Mitral atresia
- Single ventricle (including double inlet left ventricle, tricuspid atresia, hypoplastic left heart, any other anatomic abnormality with a functionally single ventricle)
- Pulmonary atresia (all forms)
- TGA (classic or d-TGA; CCTGA or l-TGA)
- Truncus arteriosus
- Other abnormalities of atrioventricular and ventriculoarterial connection (i.e., crisscross heart, isomerism, heterotaxy syndromes, ventricular inversion)

PHYSIOLOGIC Stage

Stage A

- NYHA FC I symptoms
- No hemodynamic or anatomic sequelae
- No arrhythmias
- Normal exercise capacity
- Normal renal/hepatic/pulmonary function

Stage B

- NYHA FC II symptoms
- Mild hemodynamic sequelae (mild aortic enlargement, mild ventricular enlargement, mild ventricular dysfunction)
- Mild valvular disease
- Trivial or small shunt (not hemodynamically significant)
- Arrhythmia not requiring treatment
- Abnormal objective cardiac limitation to exercise

Stage C

- NYHA FC III symptoms
- Significant (moderate or greater) valvular disease; moderate or greater ventricular dysfunction (systemic, pulmonic, or both)
- Moderate aortic enlargement
- Venous or arterial stenosis
- Mild or moderate hypoxemia/cyanosis
- Hemodynamically significant shunt
- Arrhythmias controlled with treatment
- Pulmonary hypertension (less than severe)
- End-organ dysfunction responsive to therapy

Stage D

- NYHA FC IV symptoms
- Severe aortic enlargement
- Arrhythmias refractory to treatment
- Severe hypoxemia (almost always associated with cyanosis)
- Severe pulmonary hypertension
- Eisenmenger syndrome
- Refractory end-organ dysfunction

PATENT FORAMEN OVALE (PFO)

PFO is defined as failure of the foramen ovale (opening between the atria in fetal circulation that allows blood to bypass the pulmonary vasculature) to close in the first few months of life, allowing a flap-like communication between the RA and LA

Epidemiology/Presentation
- PFOs are common (25-30% of the general population) and generally asymptomatic
- PFOs are more common (~40%)[2] in patients presenting with cryptogenic stroke, especially in those who suffer strokes before age 55
- Very rarely do PFOs result in right-to-left shunting and hypoxia, or orthodeoxia (positional desaturation)
- PFOs should be screened for in the setting of a cerebral ischemic event in young patients or hypoxemia of uncertain origin
    - Associated atrial septal aneurysms (ASA) confer highest risk for recurrent PFO-related stroke[5]

Exam: Typically normal

Imaging: Echocardiogram with color flow Doppler or agitated saline contrast (a "bubble study") is the diagnostic test of choice.

- TEE has higher sensitivity than TTE for the detection of PFO

Management

- *Primary prevention* of stroke in patients with a PFO is not indicated[3]
- *Secondary prevention* in patients with ischemic stroke/TIA and found to have PFOs and without alternative explanation for stroke despite thorough evaluation:
    - For patients aged ≤60 yrs: percutaneous PFO device closure in addition to antiplatelet therapy, rather than antiplatelet therapy alone[4]
    - For patients > 60 yrs: data less clear, as the risks of intervention must be balanced with changing technology (including percutaneous suture options)[6]
        - This does not apply to selected patients with strong clinical evidence of paradoxical embolus (ex: pts with acute DVT, PE, or other VTE)

References:

1. Stout KK et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease. J am Coll Cardiol. 2018;73(12):1494-1563.
2. Lechat et al. Prevalence of patent foramen ovale in patients with stroke. N Engl J Med. 1988; 318:1148-1152.
3. Messé et al. Practice advisory update summary: Patient foramen Ovale and secondary stroke prevention: Report of the Guideline Subcommittee of the American Academy of Neurology. Neurology. 2020; 94 (20).
4. Mojadidi et al. Cryptogenic Stroke and Patent Foramen Ovale. J Am Coll Cardiol. 2018; 71:1035-1043.
5. Turc et al. Atrial septal aneurysm, shunt size, and recurrent stroke risk in patients with patent foramen ovale. J Am Coll Cardiol. 2020; 75(18):2312-2320.
6. Gaspardone and Sgueglia. Cryptogenic stroke over 60 years of age: should patent foramen ovale be closed? Eur Heart J Supplements. 2020; 22: E82-E86

ATRIAL SEPTAL DEFECT

ASDs represent a persistent communication between the RA and LA due to abnormalities of atrial septal development and tissue regression.
There are four main types:

- Primum defect (15-20%): Also known as partial or complete AV canal defects or endocardial cushion defects. Often associated with AV valve anomalies (cleft mitral valve)
- Secundum defect (70-75%): The most common ASD. They vary in size and are usually isolated lesions but can be associated with other ASDs
- Sinus Venosus defect (5-10%): Occurs at the juncture of great veins to atrial septal tissue due to failure of correct insertion of the IVC or SVC
- Coronary sinus defect (very rare): Caused by absence (full or partial) of the wall between the coronary sinus and the LA

Epidemiology/Presentation

- Most common type of congenital heart lesion
- 2:1 female to male predominance
- Typically, left-to-right atrial shunt (due to RV compliance)
    - Can eventually lead to R-sided volume overload, RV enlargement and pHTN (rarely with large defects, right-to-left shunting and Eisenmenger Syndrome)
        - In right-to-left shunting, increased risk of paradoxical embolization and stroke

Exam: Large ASDs may result in a fixed and split S2 that does not vary with inspiration. A soft systolic crescendo-decrescendo systolic pulmonary flow murmur may be heard due to increased flow over the pulmonary valve. Precordial lift may be felt in cases or RV enlargement. Prominent P2 may be present at the apex if resting pulmonary hypertension has developed.

Imaging:

- TTE generally first step, sinus venosus defects can be difficult to diagnose by TTE but RV enlargement without other explanation should prompt additional imaging
- TEE, cardiac CT, or MRI may additionally be performed to help define the margins of the defect (an important consideration for device closure of secundum ASD) and to identify associated pulmonary venous anomalies

Management

ASD repair (primum or secundum, either transcatheter or surgical) is indicated (Class I recommendation),[1] if:

- The patient exhibits impaired functional capacity, has RA and/or RV enlargement, and net left-to-right shunting large enough to cause physiologic sequelae

ASD closure is NOT recommended (Class III: Harm) if:

- PA systolic pressure > 2/3 systemic pressure and PVR >2/3 SVR
- There is net right-to-left shunt

Note: All sinus venosus, primum, and coronary sinus defects must be repaired surgically. For isolated secundum defects, percutaneous closure is the most common approach for repair, with extremely high success rates (surgical repair reserved for very large defects or patients with deficient septal rims).

References:

1. Stout KK et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease. J am Coll Cardiol. 2019;73(12):1494-1563.

VENTRICULAR SEPTAL DEFECT

VSDs results from the failure of septal development. There are four main types:

- Supracristal (5%): Result from deficiency of the septum inferior to the aortic and pulmonary valves. Aortic valve cusp can prolapse into the VSD, leading to progressive AR and occasionally aortic sinus dilatation
- Perimembraneous (60-70%): Most common, located near the membranous septum below the AV
- Muscular (10%): Can be small or large, single or multiple, and may spontaneously close. In adults, they are generally small
- Inlet (rare): Results from deficiency of the inlet septum located beneath both mitral and tricuspid valves. Does not result in mitral or tricuspid regurgitation unless associated with an AV canal defect and septum primum defect (often seen with Down's syndrome)

Epidemiology/Presentation

- VSDs are among the most common congenital heart entities in early childhood, but only account for 10% of ACHD. Most close spontaneously.
- Small restrictive VSDs rarely cause chamber enlargement
- Moderate VSDs result in left heart volume loads (via L to R shunting)
- Large VSDs can lead to L-to-R shunting—enough to cause biventricular failure, RV volume overload, pHTN, and even reversal of flow (R-to-L shunting, i.e. Eisenmenger Syndrome)
- Note: Congenital VSDs differ from post-infarct VSDs; which typically are muscular, large, and impact RV function primarily.

Exam: Small VSDs may be associated with a high-pitched pansystolic murmur. Larger VSDs tend to cause lower-frequency murmurs or may not be audible. These should augment with hand-grip (due to increased left ventricular afterload and increased shunt fraction).
**The presence of a diastolic murmur in a patient with known restrictive VSD must be further evaluated (aortic regurgitation or aortic fistula).

Imaging: TTE is generally sufficient to define the lesion and assess for biventricular size and function.

Management

- Class I indication for repair[1]:
  - Evidence of LV volume overload and hemodynamically significant shunt AND PA systolic pressure < ½ systemic systolic pressure and PVR < 1/3 SVR
- Class II indication for repair[1]:
  - Worsening aortic regurgitation due to VSD (Class IIa)
  - History of infective endocarditis caused by VSD (if not otherwise contraindicated) (Class IIb)
  - There is net L-to-R shunt when PA systolic pressure > ½ systemic systolic pressure and/or PVR > 1/3 SVR
- Repair contraindicated (Class III: Harm)[1]:
  - PA systolic pressure > 2/3 systemic pressure, PVR > 2/3 SVR, and/or there is net R to L shunt

References:

1. Stout KK et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease. J am Coll Cardiol. 2018;73(12):1494-1563.

COARCTATION OF THE AORTA

Coarctation of the Aorta (CoA) is characterized by discrete or diffuse narrowing of the aorta. The typical location is in the region of the ligamentum arteriosum, adjacent to the origin of the L subclavian artery.

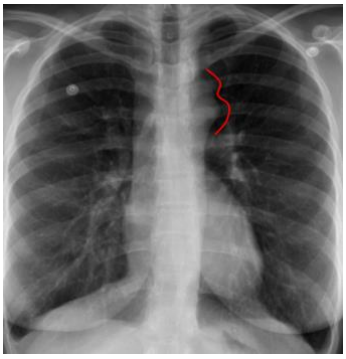
Epidemiology/Presentation[2]

- Accounts for ~5% all congenital heart defects
- Occurs more commonly in males
- Can be associated with other congenital cardiac lesions
    - In children, CoA is often associated with complex congenital heart lesions
    - In adults, bicuspid aortic valve is the most common associated defect
- Obstruction to blood flow causes increased afterload on the LV leading to LV hypertrophy
- There is also differential hypertension, with higher BP in vessels proximal to the obstruction and relative hypotension distally (patients may suffer from claudication).
- Patients are at increased risk of aortic dissection, particularly with pregnancy. 10% of CoA cases have aneurysms along the Circle of Willis (as below, should be screened with a one-time MR/CTA).

Exam: Differential hypertension can be pressure (> 20mmHg BP difference between arm and leg). Lower extremities may have diminished or late pulses (brachiofemoral delay). Systolic bruit may be heard along the scapular region. Systolic click of a bicuspid aortic valve may be heard if present (about 50-60%)

Imaging:

- CXR may show aortic indentation at the CoA site "3 sign," (see Figure) and notching on the underside of the ribs from collateral vessels
- TTE views from the suprasternal notch can demonstrate a narrowed aortic lumen as well as measure pressure gradient across the CoA segment
- CT/MRI preferred for screening for late complications (aneurysm, focal dissection, re-stenosis) and for helping guide interventional approach



Management[1]

- Class I indication for surgical repair:
    - Adults with native or recurrent CoA who have hypertension and significant native/recurrent coarctation
- Type of repair varies based on anatomy
    - Percutaneous stent implantation or surgical repair is procedure of choice, though balloon angioplasty can be considered if stent/surgical repair not feasible

References:

1. Stout KK et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease. J am Coll Cardiol. 2019;73(12):1494-1563

2. Baumgartner H et al. ESC guidelines for the management of grown-up congenital heart disease. Eur Heart J 2010;31:2915–57

Tetralogy of Fallot

Tetralogy of Fallot (TOF) is a constellation of four abnormalities: pulmonic stenosis, VSD, overriding aorta, and right ventricular hypertrophy

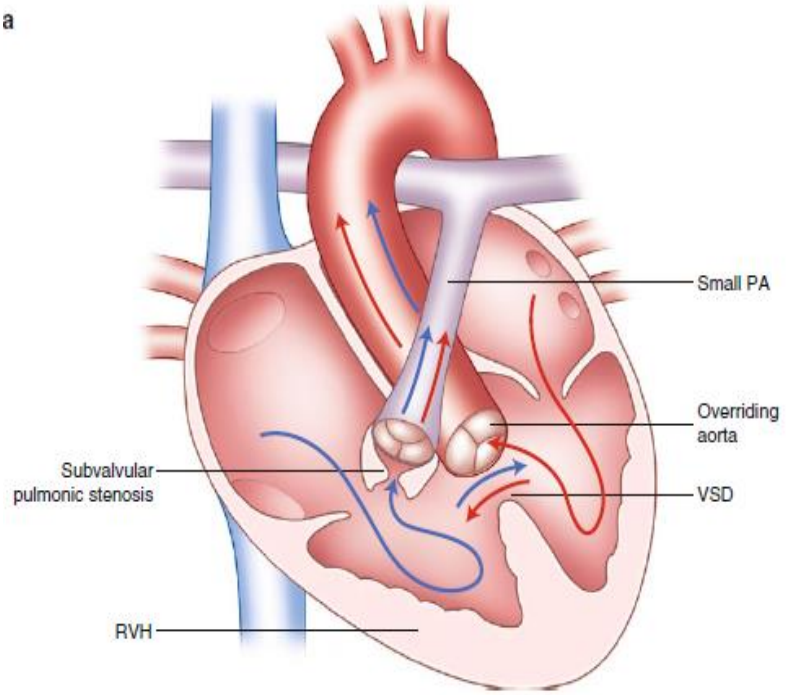


Figure 1. Native anatomy in TOF (*Adult Congenital Heart Disease in Clinic Practice*

Epidemiology/Presentation

- Initial diagnosis and management typically occurs by early childhood
  - Most patients in the current era have undergone surgical repair early infancy
  - Some older adult patients may have undergone palliative shunting prior to surgical repair
- It is the most common palliated complex CHD in adults

Exam:

- Findings in adults are variable and will depend on prior management (e.g. repair versus palliative shunt).
- Scar anatomy is important (thoracotomy and/or sternotomy)
- Many patients will have systolic RVOT murmur and patients with PR will have a diastolic murmur.
- Diminished radial pulse may indicate prior BT shunt.
- Right heart failure exam is critical (JVP, ascites, leg edema, right heart gallops)

Imaging:

- TTE is first line imaging and used to assess the degree of pulmonary regurgitation and other associated residual defects (VSD, pulmonic stenosis, aortic dilation)
- Cardiac MRI is the gold standard for following RV size and function and pulmonic regurgitation quantification and to assess for indications for pulmonary valve replacement (performed once RV volumes reach a certain size).

Management[1]

- Management in adulthood is primarily aimed at addressing late complications after childhood surgical repair including pulmonic insufficiency, recurrent pulmonary stenosis, complications of prior shunts, and arrhythmia
  - Many patients require repeat pulmonary valve intervention during adulthood (either surgical or transcatheter). Note: the origins and proximal courses of coronary arteries *must* be mapped prior.
  - Even after repair, adult pts with TOF are at increased risk of heart failure and sudden cardiac death (~2% per decade of life), which may require ICD for primary or secondary prevention as well as targeted anti-arrhythmics and/or ablation

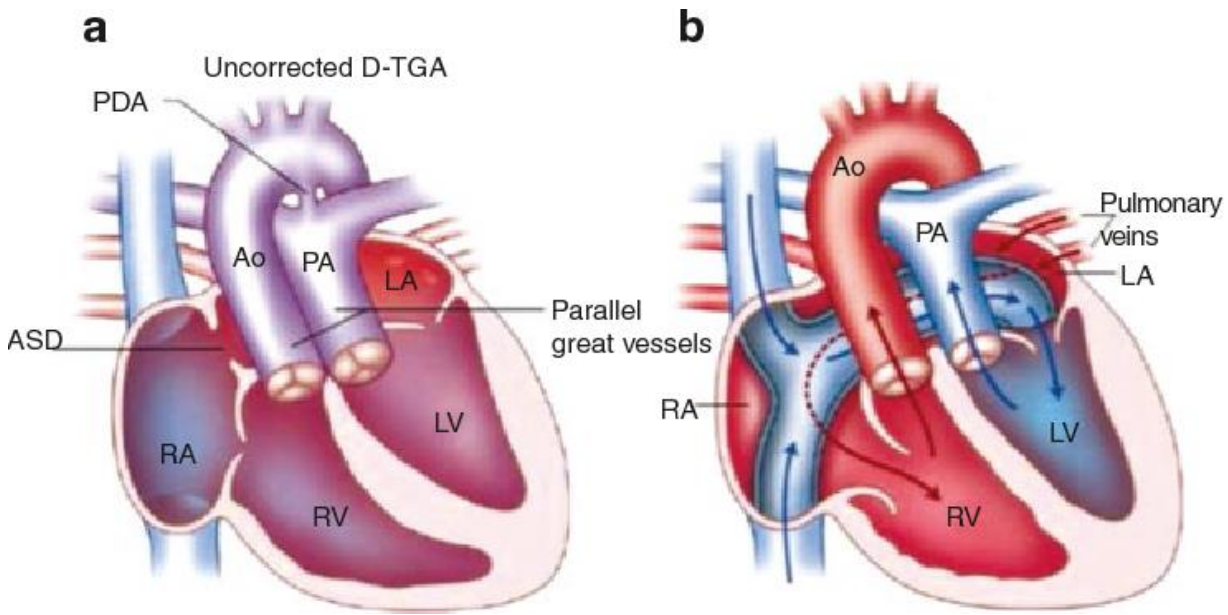
TRANSPOSITION OF THE GREAT ARTERIES

There are 2 types of Transposition of the Great Arteries (TGA): D-TGA and L-TGA

- D-TGA ("dextra-TGA"): aorta arises from anterior of the RV and the PA arises from the LV such that the RV is the systemic ventricle (deoxygenated blood is in systemic circulation, oxygenated blood is in the pulmonary circulation). Thus, systemic and pulmonary circulations are in *parallel*
- L-TGA ("levo-TGA"): in this "congenitally corrected" type of TGA, the morphologic RV is on the left and the morphologic LV is on the right, the pulmonary artery arises from the right sided LV and the aorta from the left sided RV, such that pulmonary and systemic circulation still occur in *series*

D-TGA

- Most common type
- Leads to neonatal cyanosis hence is typically corrected in childhood
    - Short-term survival is dependent on mixing of these circuits via PFO, ASD, VSDs, and/or a patent ductus arteriosus
- Adults who survive have generally undergone one of these surgeries in early life:
    - Atrial switch (Senning/Mustard procedure; see Figure 2)
        - Residual complications include baffle leak/obstruction or progressive systemic RV dilation/dysfunction after years of pumping against a systemic circulation.
    - Arterial switch (Jatene procedure, see figure 3 below)
        - Residual complications from this procedure include pulmonary branch stenosis (due to tension from anterior surgical translocation of the main PA), aortic regurgitation of the neo-aortic valve, and coronary artery stenosis as a result of surgical translocation



From Adult Congenital Heart Disease in Clinic Practice (DeFaria Yeh & Bhatt)

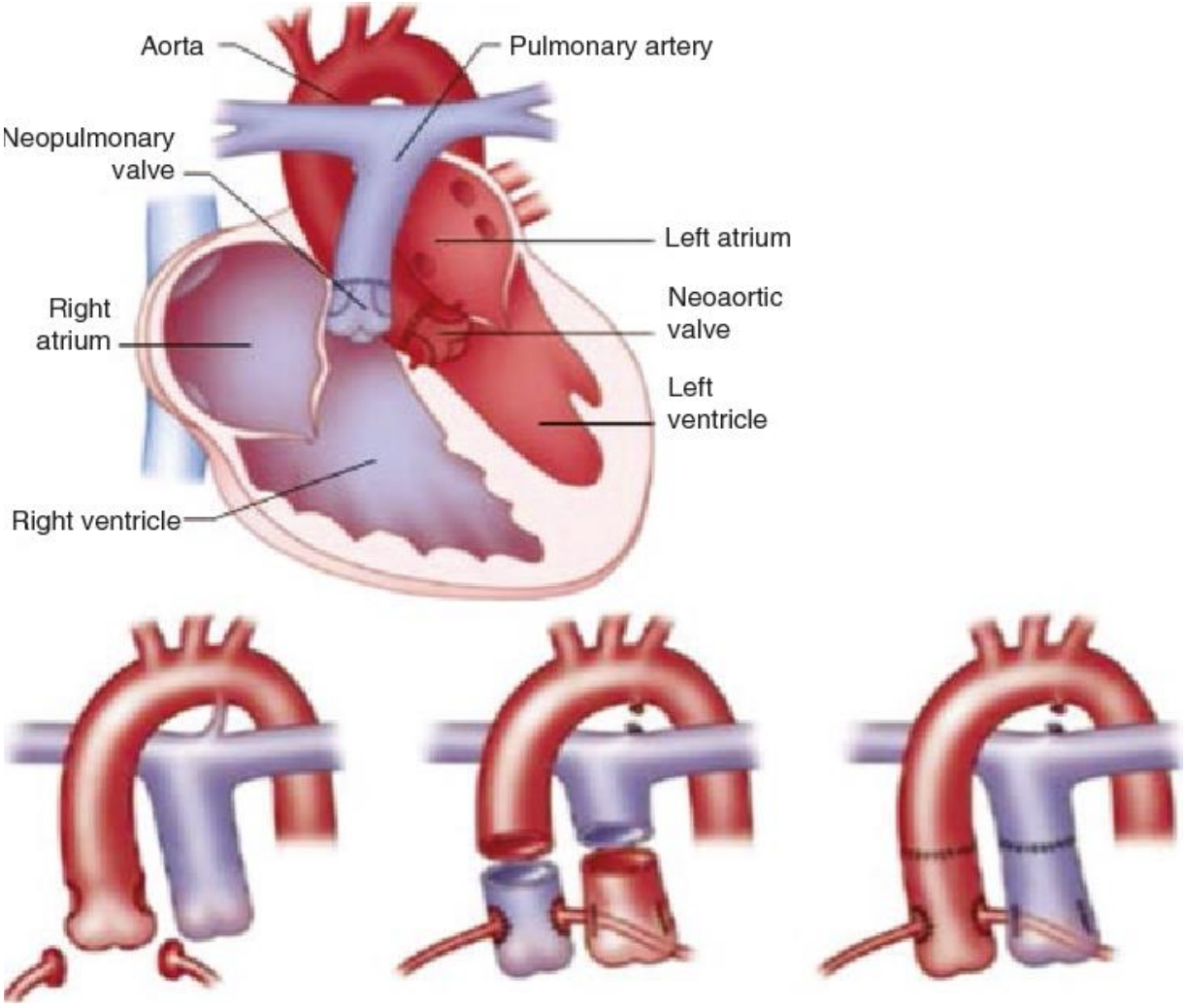
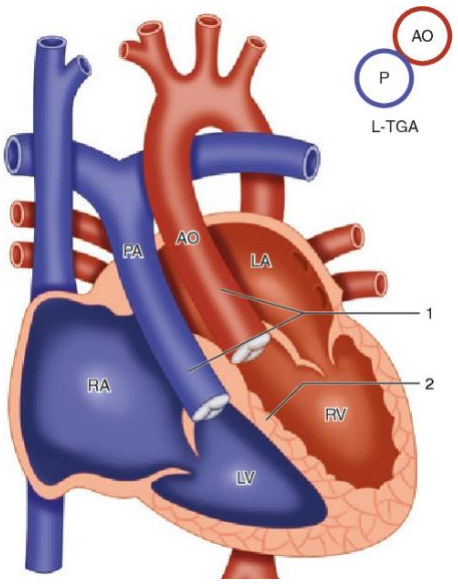


Figure 3: Jatene Procedure for D-TGA

L-TGA

- Because this is a "congenitally corrected" anomaly (ie systemic and pulmonary circulation are in series), patients may present in adulthood
  - Some adult patients will have undergone surgical correction in childhood
  - May be picked up earlier in life if associated PS/VSD where murmurs may lead to TTE
- L-TGA can be associated with other congenital anomalies such as VSD, pulmonary stenosis, apical displacement of systemic tricuspid valve, and displacement of the AV node with accessory AV node pathways (this often leads to complete heart block and/or re-entrant SVTs).
- Heart block is common: 2% development per year



From Adult Congenital Heart Disease in Clinic Practice (DeFaria Yeh & Bhatt)

Exam: In both D-TGA and L-TGA the exams will be highly variable based on prior surgical corrections and/or associated congenital anomalies

Imaging: In both D-TGA and L-TGA, cardiac MRI generally provides the best assessment of structural and functional complications. Cardiopulmonary exercise testing is important to assess peak VO2 which is highly prognostic.

Management

- Management of the adult patient with *D*-TGA involves managing complications of prior intervention
  - Arrhythmia: Ambulatory monitoring for bradycardia or sinus node dysfunction (especially true of pts treated with beta blockers/other rate-slowing medications).[1] Otherwise, standard targeted anti-arrhythmics and ablation procedures advised.
  - Baffle obstruction/leak: May present as edema of the face and upper extremities with superior baffle limb obstruction. If the inferior baffle limb is obstructed, cirrhosis and ascites may develop. These patients may also exhibit desaturation or paradoxical embolization if baffle leaks occur. Leaks/obstruction can be corrected percutaneously or surgically. Cardiac MRI provides the best assessment of structural and functional complications.
  - Progressive systemic RV dysfunction: Manage as per any other pt with RV dysfunction
- Management of the adult patient with *L*-TGA involves management of complications including arrhythmia and hemodynamic effects
  - Arrhythmia: As a result of AV nodal displacement, patients are at high risk for CHB. Many will require pacemaker implantation (in subpulmonary LV). Ablation may also be necessary for accessory pathways contributing to AVRTs
  - Progressive systemic right ventricular dysfunction: Pts are at risk of severe systemic TR due to anterior leaflet dislocation, and TV repair can be considered in rare situations. In many cases, if systemic RV failure develops then transplantation must be entertained.

References:

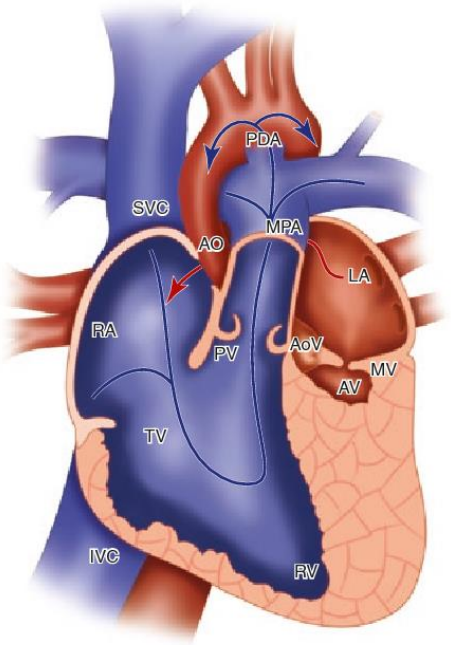
1. Stout KK et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease. J am Coll Cardiol. 2019;73(12):1494-1563

SYSTEMIC VENTRICLE PHYSIOLOGY/FONTAN PALLIATION:

see diagrams at the end of this section

- Single ventricle physiology can result from many underlying congenital heart defects that necessitate mixing.
- The four most common are tricuspid atresia, hypoplastic left heart syndrome, double inlet LV, and unbalanced AV canal defect.
- In all these native anatomies, the myocardial mass receives cardiac inflow, mixes oxygenated and deoxygenated blood, and distributes moderately oxygenated blood to both pulmonary and systemic circulations. Having moderately oxygenated blood perfusing the systemic circulation has long term consequences
- Surgical correction with the Fontan procedure aims to separate oxygenated from deoxygenated blood by routing the systemic veins directly to the pulmonary artery, the pulmonic valve is ligated and the systemic ventricular mass pumps oxygenated blood out the aorta.

Hypoplastic Left Ventricle



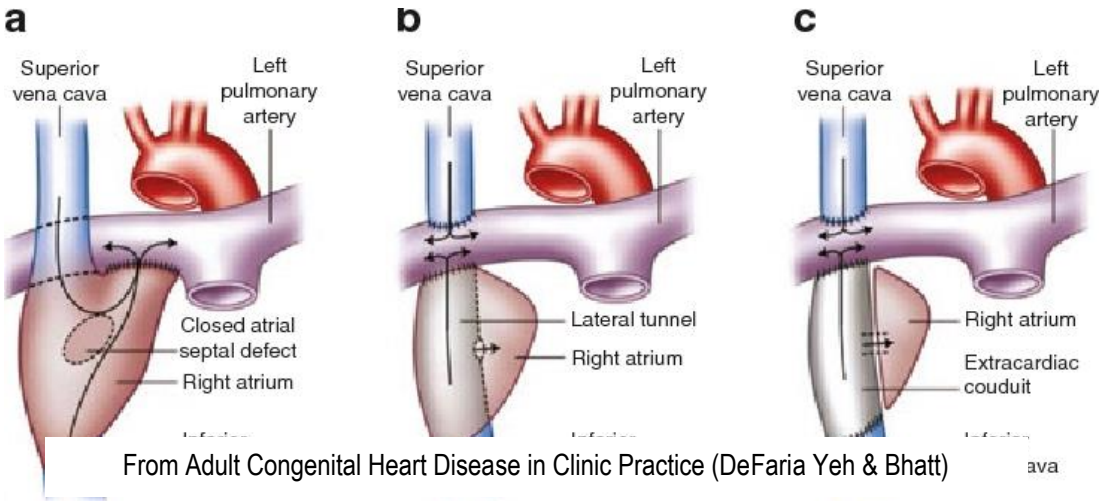
RA - Right atrium	MPA - Main pulmonary artery
RV - Right ventricle	Ao - Aorta
LA - Left atrium	SVC - Superior vena cava
LV - Left Ventricle	IVC - Left Ventricle
TV - Tricuspic valve	ASD - Atrial septal defect
MV - Mitral valve	VSD - Ventricular septal defect
AoV - Aortic valve	
PV - Pulmonary valve	

From Adult Congenital Heart Disease in Clinic Practice (DeFaria Yeh & Bhatt)

Clinical Presentation in Adults:

- Several surgeries may occur in early childhood: (***see below for diagram)***
  - 1) correcting pulmonary blood flow with pulmonary artery band or BT shunt
  - 2.) connection of the SVC to pulmonary artery (Glenn or superior cavopulmonary anastomosis)
  - 3) diversion of the IVC blood to the pulmonary artery (Fontan completion, most common in modern era is lateral tunnel)
- Careful understanding of all operative anatomy and procedures is critical to appropriate management
- After Fontan palliation, the patient lacks sub pulmonary pump to drive blood into the pulmonary arteries causing cardiac output to be limited by 1) the downstream systemic ventricle's ability to pull blood through the pulmonary bed and 2) the passive return from the systemic veins to the pulmonary artery through the Fontan circuit
  - Limited cardiac output results in exercise limitation and fatigue
  - Venous collaterals may develop between the systemic (blue) and pulmonary (red) veins, bypassing the pulmonary bed and resulting in systemic cyanosis
- Atrial arrhythmias are common
- Pts with morphologic RV pumping systemically develop early progressive ventricular dysfunction
- Patients can also develop Congestive Fontan hepatopathy leading to progressive Fontan Associated Liver Disease (FALD) and HCC

Fontan Procedure: (a) RA to PA connection (b) lateral tunnel, intracardial (c) extracardiac Fontan



From Adult Congenital Heart Disease in Clinic Practice (DeFaria Yeh & Bhatt)

Management

- Patients with Fontan circulation must be managed in conjunction with specialists in ACHD
- Fenestrations (between the Fontan lateral tunnel and systemic circuit) can be created which allow a small right-to-left shunt to persist
  - Benefits include increased cardiac output due to increased systemic preload and decreased central venous pressures
  - Downside is that fenestration is associated with increased risk of paradoxical thromboembolism
  - Hypoxemia/cyanosis may also occur in cases of excessive right greater than left shunting
- Common complications:
  - Arrhythmia: Atrial dysrhythmias are common and poorly tolerated. Targeted antiarrhythmics, ablation procedures, and ultimately conversion to extra-cardiac conduit may be indicated
  - Cyanosis: Cross sectional imaging (CTA or MRI) plus RHC should be performed to look for systemic to pulmonary venous connections, which may be treated by transcatheter occlusion
  - Thrombosis: Fontan physiology represents a low-flow state, and the degree of right-to-left shunting in these patients makes systemic thromboembolism a very high risk. Anticoagulation is indicated if there is history of atrial arrhythmia, fenestration, or EF <40% (even in patients without history of thromboembolism)
  - Protein-losing enteropathy: Though the pathophysiology is poorly understood, this is a complication occurring in 3-18% of patients. Mortality is very high with only ~50% 5-year survival. Therapy is empiric and includes optimizing Fontan hemodynamics, considering fenestration, optimizing cardiac output, and reducing pulmonary vascular resistance
  - Spontaneous fenestration closure: This occurs frequently and may be a silent event. However, in patients with poor cardiac output who were dependent on fenestration to augment ventricular preload, cardiac output may drop, systemic venous pressures may rise, and protein-losing enteropathy may ensue
  - Heart failure: Symptoms may progress such that transplantation may be the only therapeutic option. Of note, early post procedure transplant outcomes within this population are poor relative to those with biventricular circulation due to anastomotic challenges and bleeding. However, if patients survive, early post procedure window survival is on par with other age-matched patients
  - NAFLD: regular screening is imperative with liver ultrasound or MRI, HCC screening

LEFT-TO-RIGHT SHUNTING AND EISENMENGER SYNDROME

There are several congenital abnormalities that cause blood to flow from the systemic to pulmonary circulation (left-to-right shunt). Rarely, large uncorrected shunts may progress to Eisenmenger physiology in which the excess flow across the pulmonary arteries from the shunt leads to pulmonary vascular remodeling and increased pulmonary vascular resistance (PVR), which results in shunt reversal (right-to-left shunting) and cyanosis.

Epidemiology and Presentation

- Adults presenting with the Eisenmenger syndrome typically have progressive dyspnea, chronic exercise intolerance, and symptoms of right heart failure
  - Even rarer: presenting with arrhythmia, syncope, hemoptysis, or cyanosis
- Systemic to pulmonary (left-to-right) shunt lesions result in volume overload, with resulting chamber enlargement (the chamber and degree of enlargement is dependent on shunt size and location)
  - Pre-tricuspid valve shunts (ASD, anomalous pulmonary venous returns) typically result in RA/RV volume overload
  - Post-tricuspid valve shunts (VSD, PDA) result in LA/LV volume overload (LV systemic output decreased by shunt -> compensatory increase in intravascular volume until LVEDV is sufficient to produce normal CO -> LV volume overload)

- In progression to Eisenmenger Syndrome, R-sided pressure overload results from both direct transmission of pressure from the higher-pressure LV as well as increased afterload due to pulmonary arterial remodeling
    - Overtime, increased PVR causes elevated right-sided pressures as the RV aims to maintain cardiac output. If right-sided pressures approximate and then exceed left-sided pressures, the shunt direction can reverse, resulting in systemic desaturation
- Rate of progression of pulmonary hypertension is dependent on the type and size of the anatomic defect, as well as the magnitude of shunt flow
    - Patients with ventricular (i.e. VSD, AVSD) or arterial shunts (i.e. PDA, truncus arteriosus) are at higher risk of progressing rapidly to Eisenmenger syndrome compared to patients with pre-tricuspid shunt lesions

Exam: Examination may reveal signs of PH and RV failure (RV heave, loud P2 that extends to apex, prominent venous a wave); chronic hypoxemia (cyanosis, clubbing); and/or TR/PR and murmur of the causative lesion (will become progressively more quiet as pulmonary and systemic pressures equalize).

Imaging: TTE should be initial diagnostic imaging (as well as CT or cardiac MR in certain cases)

Management

Eisenmenger syndrome patients must be managed in conjunction with an ACHD specialist

- Care of patients with Eisenmenger syndrome includes avoidance of the following (Class I recommendations)[1]:
    - Significant volume shifts (dehydration, or volume overload)
    - Chronic exposure to high altitude
    - Iron deficiency
    - Strenuous activity (in particular, isometric exercise)
    - Excessive heat (i.e. sauna, hot tub) due to risks associated with dehydration as well as worsening of right-to-left shunting through systemic vasodilation
    - Unnecessary surgery or anesthesia
    - Pregnancy (high maternal mortality)
- These pts require prompt workup and treatment for infection, as they may not have the cardiac reserve to support septic physiology
    - Systemic vasodilation will worsen right-to left shunt flow

- Any degree of pulmonary hypertension should be appropriately managed
    - See AHA/ACC 2018 ACHD guidelines for full recommendations and specific therapies. Mortality benefit is conferred with pulmonary vasodilator therapy
        - Bosentan is Class I recommendation for Eisenmenger + ASD or VSD
        - PDE-5 inhibitors have Class IIa recommendation to treat for Eisenmenger + ASD or VSD
- The only surgical option for patients who have progressed to Eisenmenger physiology is heart-lung transplant. Bilateral lung transplant with intracardiac repair is less common.
- Additional management considerations relate to various complications. Common complications in these patients include:
    - Arrhythmia/SCD: Patients are at increased risk of both atrial and ventricular tachyarrhythmia. Endocardial pacing, if necessary, is not recommended in intravascular shunting due to risk of paradoxical emboli and infection
    - Hypoxemia: Due right-to-left shunting. Generally, avoid intubation due to temporary hypoxemia in the setting of anesthesia
    - Hemoptysis: Secondary to pulmonary vascular hypertension (risk of bronchial artery rupture)
    - Thrombosis: Pulmonary arterial thrombi are often seen and are associated with worse disease. However, the use of oral anticoagulants is controversial given the risk of hemoptysis as above. In the absence of reliable data, oral anticoagulant therapy may be carefully considered in patients with severe disease and no prior episodes of hemoptysis.
    - Paradoxical embolism: Filtering of all IVs is essential to prevent strokes. Avoidance of central lines and endocardial pacer leads is also encouraged to reduced risk of VTE and paradoxical embolism
    - Erythrocytosis/Hyperviscosity: Secondary erythrocytosis is common given physiologic response to chronic hypoxemia. Resulting hyperviscosity may contribute to the increased risk of neurovascular events. Therapeutic phlebotomy should be performed only when neurologic symptoms are attributed to hyperviscocity and hemoglobin is > 20 g/dL or hematocrit is > 65%.
        - Iron deficiency and dehydration must be excluded before phlebotomy is considered. Iron deficiency worsens intravascular sludging and increases risk of stroke. CBC and iron stores should be checked at least yearly and repleted as necessary

- Hyperuricemia: Increased uric acid levels are common in patients with cyanotic congenital heart disease and are due to increased production and decreased renal clearance. Serum uric acid increases in proportion to hemodynamic severity in adults with Eisenmenger syndrome and is associated with long-term mortality. Uric acid levels should be assessed annually, and treatment of hyperuricemia should be initiated in patients who develop gout.

References:

1. Stout KK et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease. J am Coll Cardiol. 2019;73(12):1494-1563
2. DeFaria Yeh et al. 2018. Adult Congenital Heart Disease in Clinic Practice

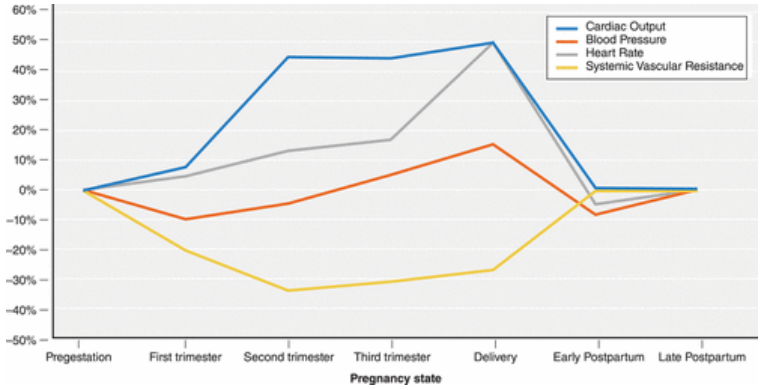
CARDIO-OBSTETRICS

Basic Physiology of Pregnancy

ANTEPARTUM

SVR: ↓ *(nadir 2T)*
HR: ↑ *(peaks in late 3T)*
Total Blood Volume: ↑ "physiologic anemia and ↑EPO"
CO: ↑ to 30-50% above baseline *(peaks in early 3T; increases due to (1) increased preload, (2) reduced afterload and (3) increased HR)*
MAP: Mild ↓ in 1+2T, returns to pre-pregnancy baseline in 3T *(balanced ↓ SVR reduction with concomitant ↑ in CO)*

Hemodynamic changes in normal pregnancy (source: AHA)



INTRAPARTUM

CO ↑ by ~15% in early labor, ~25% in active phase of labor, ~50% during pushing in second stage. *Note: Epidural anesthesia attenuates some of this increase.* Uterine contraction contributes 300-500cc blood/contraction into maternal circulation.

POSTPARTUM

Immediately post-partum CO ↑ to 80% above pre-labor value due to autotransfusion from aortocaval decompression/uterine involution (blood auto-transfused usually > blood lost during labor). BP should remain constant during this phase, hypotension is abnormal. Returns to baseline over ~ 3 months.

NOTE: hypotension in third trimester may be due to positioning or volume depletion

Supine Positioning → hypotension 2/2 compression of aorta and vena cava due to gravid uterus (reduced CO and SV, increases HR) → place in left lateral decubitus shifts uterus off major vessels → restoration of venous return, CO → improved BP

Risk stratification of women with pre-existing cardiovascular disease interested in pregnancy

1. Modified WHO classification (most commonly used; 2018 ESC guidelines). Population specific: CARPREG, ZAHARA, ROPAC (Regitz-Zagrosek et al. EHJ 2018, 39(34): 2165-3241)

Cardiac Diagnosis in Pregnant Women

Exam

Normal: Higher basal heart rate; JVP normal to mildly elevated, loud heart sounds, S3 and venous hum/mammary flow, splitting of S1 or S2 in 3T
Abnormal: S4, diastolic murmurs, signs of CHF, loud P2 or RV heave

Studies

Echo: **Normal**: physiologic multivalvular regurgitation (R>L) during late gestation, can persist into early postpartum. Chamber enlargement, annular dilatation, small physiologic pericardial effusions are frequent incidental findings during pregnancy. **Abnormal**: AR, large effusion, symptoms of pericarditis
EKG: **Normal**: 15-20 degree LAD, enlarged chamber volumes. Q waves in III and aVF, TWI in III, V1-V3. PACs and PVCs common.
Labs: NT-proBNP doubles but remains within normal limits. Low NT-proBNP has strong NPV for CV complications (Tanous et al. JACC 2010; 56(16);1247-53)

If imaging is required for workup during gestation, talk with our OB colleagues to help engage your patient in an informed risk/benefits conversation. Most imaging studies do not carry significant risk to mom or fetus, and it is very important to make the correct diagnosis in a pregnant women (i.e. etiology of troponin elevation should be determined, PE should be evaluated with CT when clinical

Manual Uterine Displacement Techniques:

1-handed from right side of pt:

INCLUDEPICTURE "https://www.ahajournals.org/cms/asset/7c6ebcf8-3c15-41ee-bf59-dff5bbf36a79/1747fig03.jpg" * MERGEFORMATINET

2-handed from left side of pt:

Figures 3&4 (Circulation 2015; 132:1747-1773)

ACLS in Pregnancy

See 2015 AHA Statement on cardiac arrest in pregnancy for more details (Circulation 2015;132:1747-1773)

- At onset of arrest **PAGE MATERNAL CARDIAC ARREST TEAM** (see ACLS algorithm below)
- **MATERNAL** interventions and **OBSTETRIC** interventions should be performed **IN TANDEM**

Maternal interventions

- Place IV above diaphragm
- If receiving IV mag, STOP mag and give calcium chloride or gluconate
- Defibrillation and epinephrine should be given when indicated according to the standard ACLS algorithm
- If you suspect PE as a cause of arrest, treat it and get PERT involved; Alteplase is not strictly contraindicated in pregnancy; heparin and LMWH are safe

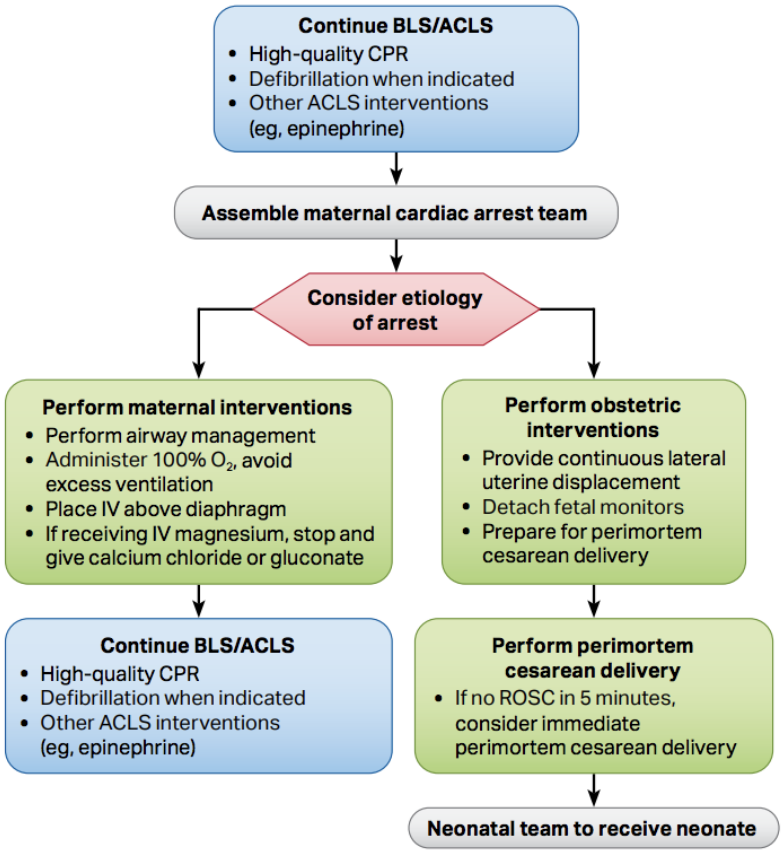
Obstetric Interventions

- While performing compressions relieve aortocaval compression with lateral uterine displacement
- If no ROSC within 4-5 minutes, consider immediate perimortem cesarean delivery. Goal is to improve both maternal and fetal outcomes

Potential Etiologies of Maternal Cardiac Arrest: ABCDEFGH

- Anesthetic complications
- Bleeding
- Cardiovascular
- Drugs
- Embolic
- Fever
- General non-OB causes (Hs & Ts)
- Hypertension

Cardiac Arrest in Pregnancy In-Hospital ACLS Algorithm



Maternal Cardiac Arrest

- Team planning should be done in collaboration with the obstetric, neonatal, emergency, anesthesiology, intensive care, and cardiac arrest services.
- Priorities for pregnant women in cardiac arrest should include provision of high-quality CPR and relief of aortocaval compression with lateral uterine displacement.
- The goal of perimortem cesarean delivery is to improve maternal and fetal outcomes.
- Ideally, perform perimortem cesarean delivery in 5 minutes, depending on provider resources and skill sets.

Advanced Airway

- In pregnancy, a difficult airway is common. Use the most experienced provider.
- Provide endotracheal intubation or supraglottic advanced airway.
- Perform waveform capnography or capnometry to confirm and monitor ET tube placement.
- Once advanced airway is in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions.

Potential Etiology of Maternal Cardiac Arrest

A Anesthetic complications
B Bleeding
C Cardiovascular
D Drugs
E Embolic
F Fever
G General nonobstetric causes of cardiac arrest (H's and T's)
H Hypertension

Cardiac Medications during pregnancy

Pharmacokinetic Changes during Pregnancy: Drug distribution and clearance may be affected. Important factors include delayed gastric emptying and motility; increased plasma volume and fat accumulation increased volume of distribution; decreased albumin and plasma binding proteins; increased hepatic and renal clearance; cytochrome P450 enzymes mostly upregulated

Pregnancy and Lactation Labeling Rule (PLLR): In 2015, PLLR replaced previous FDA scoring system of medications (used to be ABCDX). Incorporates consideration that baseline rate of major birth defects and miscarriage, and includes recommendations for pregnancy, labor, delivery and lactation all on the same label. New system more descriptive than prior ABCDX approach.

Guiding principles: Consider necessity, urgency, timing during gestation, fetal adverse effect of drug. **Use lowest effective dose**. Counsel re: limited availability of data, when pertinent. MFM should help guide intrapartum and post-partum medications.

Summary of safety during pregnancy for the most commonly used cardiac medications (adaptation of central illustration from Halperin et al, see original paper for further discussion as well as FDA categorization and lactation safety) (Jeejeebhoy et al. Circulation 2015; 132(18); 1747-73)

•	Arrythmias	Heart Failure/Shock	HTN/PHTN	Heme
Contraindicated	Amiodarone	Aldosterone antagonists Atenolol ACEi, ARB	Atenolol ACEi, ARB Endothelin-R antag	Statins DOAC
Considered Safe	Adenosine Digoxin Lidocaine Metoprolol Propranolol	Metoprolol Carvedilol Furosemide Dopamine Dobutamine Norepinephrine	Labetalol Nifedipine Alpha-methyldopa (PO)	UFH Enoxaparin
Limited data/ to be used with caution	Verapamil Diltiazem Procainamide Sotalol Flecainide Propafenone	Hydralazine Isosorbide dinitrate Nitroglycerin Metolazone Torsemide	Amlodipine Hydralazine Iso dinitrate Iloprost Epoprostenol Nitroglycerin Nitroprusside Sildenafil	Alteplase ASA 81mg Clopidogrel Warfarin Argatroban Bivalirudin Fondaparinux Prasugrel Streptokinase Ticagrelor

Peripartum Cardiomyopathy (PPCM)

Definition: (1) cardiomyopathy presenting with HF secondary to LV systolic dysfunction (EF<45%) (2) towards the end of pregnancy or in the months following delivery (3) with no other evident cause (diagnosis of exclusion) (Silwa et al. Eur J Heart Failure 2010; 12:767-778).

Incidence: PPCM seen in ~103/100k births in the United States with marked regional variation across the world, maternal mortality rate ~ 14/100k of live births (Kolte et al. JAHA 2014; 3(3):e001056)

Risk factors: Age > 30 y.o, African descent, pregnancy with multiple fetuses, hx of PEC, eclampsia or postpartum HTN, longterm tocolysis (Lee et al. Circ Heart Fail 2018; 11(4):e004134)

Pathophysiology: dysregulated metabolic pathways and angiogenic imbalance. Prolactin regulation (via STAT pathway) and VEGF (in PGC-1a KO murine models and via sFlt1 antagonism) regulation implicated (Hoes et al. Nat Rev Cardiol 2022; doi: 10.1038/s41569-021-00664-8).

Diagnosis: Most often first month postpartum. **S/Sx**: dyspnea, pedal edema, orthopnea, PND, chest tightness. *Note: do not dismiss pedal edema and SOB symptom of pregnancy, especially post-partum* (Arany et al. Circulation 2016; 133(14):1397-409). **Work-up**: NTproBNP, TTE, can obtain cMR but avoid gadolinium during pregnancy, no EMB unless high suspicion for other etiology.

Management: Similar to other forms of HFrEF (see position statement from HF Association of the ESC for details) i.e. GDMT; continue if EF remains depressed, however no data to support duration of tx after EF recovery (see figure below). *Important points*: **Anticoagulation**: Consider when LVEF<30-35% during late pregnancy and 6-8 weeks postpartum. Favor LMWH over warfarin (unless mechanical heart valves), both safe with lactation. No data for DOACs, avoid (Davis et al. JACC 2020; 75(2) 207-221). **Experimental:** Bromocriptine in addition to standard therapy is associated with a higher

rate of EF improvement, although no difference in overall rates of recovery in several small trials. (Silwa et al. Circulation 2010; 121:1465-1473; Yaméogo et al. J Cardiol Clin Res 2017; 5:1098-1106; Hilfiker-Kleiner et al. Eur Heart J 2017; 38:2671-2679). Ongoing REBIRTH trial of 200 women with PPCM to further evaluate bromocriptine in PPCM on myocardial recovery. ESC 2018 guidelines include Class IIb recommendation for bromocriptine; if used, must also consider therapeutic AC in conjunction due to elevated thrombotic complication risk. **Advanced therapies:** 60% of cardiogenic shock during or after pregnancy are related to PPCM (Banavan et al. Hypertens Pregnancy 2017; 36:117-123). tMCS and ECMO should be considered early. **Lactation:** Current data suggest breastfeeding safe in PPCM, in spite of stimulation of prolactin secretion (Koczo et al. JACC Basic Trans Science 2019; 4:291-300). **Primary PPX for sudden cardiac death:** Because PPCM has higher likelihood of recovery of EF, important to avoid premature ICD; consider wearable vest in severely reduced LVEF until recovery or ICD placement. **Subsequent pregnancy:** as illustrated below, risk is stratified by recovery of EF; persistent systolic dysfunction portends high risk pregnancy.

MEDICATION	DURING PREGNANCY	POTENTIAL ADVERSE EFFECTS	INDICATIONS	DURING LACTATION
HEART FAILURE MEDICATIONS				
Loop diuretics	Yes	Caution for hypovolemia or hypotension that may lead to decreased placental perfusion	For signs and symptoms of congestion and fluid overload.	Yes, but over-diuresis can lead to decreased milk production.
Beta blockers (metoprolol tartrate used most commonly)	Yes	IUGR; fetal bradycardia and hypoglycemia	For standard treatment of HF; consider treatment of women with subsequent pregnancy.	Yes
Hydralazine/nitrates	Yes	Caution with hypotension	Use for afterload reduction during pregnancy (instead of ACE-I/ARB) when needed.	Yes, but ACE-I/ARB typically chosen post-partum
Digoxin	Yes	No associated congenital defects	Can be used with symptomatic heart failure and/or systolic dysfunction during pregnancy, or afterwards per guidelines.	Yes
ACE-I/ARB	No	Anuria, oligohydramnios, fetal limb contractures, craniofacial deformation, pulmonary atresia, fetal hypocalvaria, intra uterine growth restriction, prematurity, patent ductus arteriosus, stillbirth, neonatal hypotension and death	Cannot use during pregnancy. After delivery, should be used as part of guideline-directed medical therapy for afterload reduction and LV remodeling.	Enalapril and captopril can be used
Aldosterone receptor antagonists	No	Spironolactone has been associated with antiadrenergic activity, feminization of male rat fetuses and permanent changes in reproductive tract in both sexes	As per guideline-directed medical therapy for heart failure.	Spironolactone can be used
Sacubitril-valsartan	No	Same as ACE-I/ARB	As per guideline-directed medical therapy for heart failure.	No information in human, present in rat milk
Ivabradine	Scant data in humans; would avoid due to concerns in animal studies	Scant data in humans, animal data suggest risk	As per guideline-directed medical therapy for heart failure.	No information in human, present in rat milk
ANTICOAGULANTS				
Low molecular weight heparin	Yes	Caution at time of delivery and with neuraxial anesthesia; does not cross placenta; consider the need for monitoring anti-Xa levels	For prevention and treatment of thromboembolic complications during pregnancy and as bridge to warfarin postpartum.	Yes
Warfarin	Avoid	Warfarin embryopathy and fetopathy	For prevention and treatment of thromboembolic complications postpartum.	Yes

Legend:

	Data or experience to support use
	Caution with using this medication
	Data is limited or inconclusive

Subsequent Pregnancy	Recovered (LVEF ≥50%)	Nonrecovered (LVEF <50%)
Preconception or First Visit	Preconception risk counseling and follow-up planning. Clinical and LVEF reassessment off renin-angiotensin blocking agents for 3 months. Baseline echocardiogram and BNP/NT-proBNP level.	Preconception risk counseling including discussion of alternative ways to build a family. If pregnant and not considering termination: Close follow-up planning, stop renin-angiotensin blocking agents and switch to hydralazine/isosorbide dinitrate. Baseline echocardiogram and BNP/NT-proBNP level.
Maternal Risks	~20% have a relapse Severe deterioration is rare Mortality unlikely Rate of subsequent recovery is high	Higher risk of relapse ~50% show further deterioration in LV dysfunction Increased morbidity and mortality Premature delivery and abortion more common
Medications	Continue beta blocker therapy (metoprolol tartrate preferred). Yield of starting prophylactic beta blocker therapy unclear. Diuretics and hydralazine/isosorbide dinitrate in case of clinical or LV functional deterioration.	Continue beta blocker therapy (metoprolol tartrate preferred). Hydralazine/isosorbide dinitrate for hemodynamic and symptomatic improvement. Consider digoxin. Consider anticoagulation if severe LV dysfunction (LVEF <35%).
Follow-up	Close monitoring of symptoms during pregnancy and the postpartum period with repeat echocardiographic assessment of LV function and BNP/NT-proBNP level at the end of the 1st and 2nd trimesters, 1 month prior to delivery, after delivery prior to hospital discharge, 1 month postpartum, and at any time if symptoms develop.	
Labor and Delivery	Multidisciplinary team for planning; patient involved. Spontaneous vaginal delivery preferred unless fetal or maternal instability. Monitor for volume overload in the first 48 hours after delivery in cases of recurrent LV dysfunction.	Multidisciplinary team for planning; patient involved. Spontaneous vaginal delivery preferred unless fetal or maternal instability. Early delivery if further decrease in LV function and hemodynamic deterioration. Consider hemodynamic monitoring for optimization prior to delivery and monitoring during and after delivery. Monitor for volume overload in the first 48 hours after delivery.

(illustrations from *JACC* State-of-the-Art Review - Davis et al. JACC 2020; 75(2) 207-221)

Prognosis: 46% of patients have LVEF recovery within 6 months of diagnosis (Hoes et al. Nat Rev Cardiol 2022; doi: 10.1038/s41569-021-00664-8). If LVEF normalizes post-partum, women still carry an increased risk of clinical HF, further deterioration in LVEF and persistent LV dysfunction with a subsequent pregnancy. If LVEF does not normalize post-partum, risks of HF, further deterioration of LVEF, persistent LV dysfunction are further increased, and importantly maternal mortality is increased with subsequent pregnancy (Elkayam JACC 2011; 58 (7) 659–670). Women should be carefully counseled about very high risks of further pregnancies (Davis et al. JACC 2020; 75(2) 207-221)

Hypertensive Disorders of Pregnancy

Disease	Diagnostic Criteria
Gestational HTN	• New onset HTN after 20w gestation, SBP >=140 or DBP >=90 on at least 2 occasions 4 hours apart • No proteinuria, no severe features of pre-eclampsia (see below)

Preeclampsia (PEC) +/- severe features	• New onset HTN after 20w gestation, SBP >=140 or DBP >=90 on at least 2 occasions 4 hours apart
	• Must have proteinuria OR in the absence of proteinuria one of the symptoms/labs below
	  ○ + Proteinuria: Spot UPro:Cr >=0.3, >=300 mg per 24h urine collection or urine dip >=1 (if no other methods available) OR
	  ○ In the absence of proteinuria, one of the following: Plt <100k, Cr > 1.1 or 2x baseline w/o other renal disease, ALT/AST> 2x ULN, pulmonary edema, persistent cerebral or visual symptoms
	• With severe features: SBP >=160 or DBP >110 on 2 occasions at least 4 hours apart while patient on bed rest OR any of the above symptoms/labs (besides proteinuria)

Eclampsia	• PEC + generalized seizures that cannot be explained by other causes
HELLP syndrome	• HTN can be seen in patients with HELLP (hemolysis, elevated liver enzymes, low platelets), but not always present nor required for diagnosis

Chronic (pre-existing) HTN	• HTN diagnosed or present before 20w gestation (also if first diagnosed during pregnancy and present for >12w post-partum)
Chronic HTN + superimposed PEC +/- severe features	• Chronic HTN with sudden increase in BP that was previously well controlled, or requiring escalation of anti-HTN regiment to control BP • New onset proteinuria or sudden increase in proteinuria if had prior to pregnancy • See severe features above

Adapted from UTD Hypertensive Disorders of Pregnancy

Risk factors: personal history of PEC, chronic HTN, age, multiple gestation, obesity, race, diabetes, renal disease, autoimmune disease.

Management:
Acute severe hypertension: reduce MAP by no more than 25% over 2h using IV labetalol 20 mg over 2 minutes (hydralazine also OK but labetalol preferred), followed at 10 min interval doses of 20 to 80 mg up to max total cumulative dose of 300 mg if BP remains above target, constant infusion can be used instead of intermittent therapy**.** If labetalol alone ineffective ACOG recommends switching to hydralazine (and vice versa). Alternative options include nicardipine and nifedipine. **If PEC or Eclampsia** → give IV mag sulfate in addition to anti-hypertensive medication. **Call OB.**
Chronic HTN → target is less than 140/90 mmHg (CHAP Trial Consortium, NEJM 2022; prior CHIPS 2015 trial suggested strict versus lax BP control were equal, but underpowered for clinical outcomes). **Meds:** First line: labetalol and nifedipine. Second line: hydralazine. Methyldopa less effective. If already on amlodipine or HCTZ, ok to continue. STOP ACEi, ARBs, MRA for teratogenicity.
Risk reduction: ASA 81mg daily during 2T and 3T reduces PEC risk. USPTF Grade B recommendation for ASA after 12 weeks gestation (similar to ACOG recommendation for ASA).

Arrhythmias in Pregnancy

Incidence: Significant ectopy (PVC, paroxysmal SVT) common. In addition, variation of SVT most common, followed by AF/AFL, VF/VT (overall 70 per 100,000) (Vaidya et al. Circulation 2017; 135(6):619-621).

Pathophysiology: hypothesized to be related to atrial stretch leading to irritated tissue and re-entrant arrhythmias. Important to control arrhythmias due to risk of impaired fetal perfusion. Sustained tachycardia not well tolerated, especially AFL.

Diagnosis and Management: diagnosis and treatment for arrhythmias in pregnancy follows same principles as in non-pregnant patients. Pregnancy may reveal index case of underlying structural heart disease or inborn arrhythmia (e.g. WPW, ARVC, HCM, etc.) **Notable points***:* adenosine and cardioversion are safe. Catheter ablation is safe, better to delay until late pregnancy or postpartum. Metoprolol, propranolol, verapamil, digoxin, lidocaine (fetal bradycardia), procainamide are preferred agents; AVOID atenolol (fetal bradycardia, IUGR, highest risk among BB although risk is shared), amiodarone (consider after 1T), dronedarone. **Lactation:** All passed into breast milk. **Anticoagulation**: Use CHAD2S2-VASc. Unclear risk of stroke with limited data (ESC Guidelines On Management of Cardiovascular Diseases During Pregnancy Eur Heart J 2011; 32(34):3147-97).

Pregnancy and Acute Coronary Syndrome

Key principle: **The fundamentals of diagnosing ACS in pregnant patient are the same as in non-pregnant patient**

There are some baseline EKG changes in pregnancy (ex: LAD 2/2 diaphragm elevation, TWI III and aVF, small Q in III) but **ST changes are never normal** (Kealey et al. Can J Cardiology 2010; 26(6): 185-9)

Management of acute MI in pregnancy: *See diagram below.* Adapted from: Ismail et al Clinical Cardiology 2017;40: 399-406
In addition, low-dose ASA (81mg), Beta Blocker (Metoprolol preferred) is safe**.** NB: Despite the appropriate role of PCI in early mgmt. of MI in pregnancy, coronary catheterization rates during pregnancy are lower than expected in ACS (Cauldwell et al Heart 2019;105(3):189-195**).**

Special case: Spontaneous coronary artery dissection (SCAD): *See 2018* 2018 AHA Scientific Statement *on management of SCAD for further details*
Most common cause of acute MI in pregnancy and most commonly occurs first week after delivery. **Dx:** Coronary angiogram is recommended. **Management**: medical management may be preferred over invasive given risk of propagating the dissection[22] especially if there is only minimal distal coronary ischemia or preserved coronary flow. PCI v

CABG should be considered in patients with ongoing ischemia, hemodynamic instability, or LM disease (Hayes et al, Circulation 2018; 137: e523-e557). Obtain arterial imaging from head to pelvis as there is an association between SCAD and fibromuscular dysplasia. **Prognosis:** SCAD treated conservatively 95% of the time will heal in one month (JACC State-of-the-Art Review. J Am Coll Cardiol 2020;76:961-984).